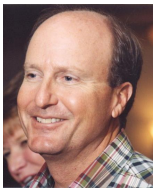


PSY 707: Biological Bases of Behavior

Joe Ferguson for Dr. Anthony Greene
October 27, 2006

General Citations

Thank you for your patience in providing me with the unusual opportunity to hold this KA open for over 3 years, during which time various other academic priorities have delayed its completion. This is my very last program requirement and my PhD will be awarded upon its completion. Completing this KA over that long a period of time has provided a unique opportunity to consider the biological bases of behavior at variable intensity over a long period of time, which I have not done with any of my other knowledge areas. My responses to the 18 questions that constitute my fulfillment of your requirements for PSY 707 are largely attributable to the following general sources, which have broadly informed my understanding of these subjects.

Two general textbooks have guided my exploration of this area, and have been my first recourse for each of the topics that are addressed in the remainder of this document. *Fundamentals of Human Neuropsychology* (Kolb & Whishaw, 2003) reflects a generally more clinical approach than *Physiology of Behavior* (Carlson, 2001), which provides a more detailed technical discussion of each topic. *Essential Pharmacology (Stahl, 2000)* provides an excellent survey of psychopharmacological issues, while *Wet Mind* (Kosslyn & Koenig, 1992), *Executive Brain* (Goldberg, 2001), and *Affect Regulation and the Origin of the Self* (Allan N. Schore, 1994) helpfully supplemented the two textbooks cited above. In addition, Wikipedia (http://www.Wikipedia.org) has been an extremely valuable resource, as has also been the *Stanford Brain Tutorial* (http://www.stanford.edu/group/hopes/basics/braintut) as well as the *Lundbeck Institute Brain Atlas* (http://www.brainexplorer.org/brain_atlas/Brainatlas_index.shtml)

1) Imagine the human brain as a high-rise executive office complex, and I am a prospective investor who is considering buying the whole complex, including the current tenants. Give me a detailed tour of the main divisions of the office tower (hint: forebrain, midbrain, hindbrain), and the names and functions of each of the subdivisions.

A phalanx of secret service agents in grey suits and dark glasses precede the arrival of the President's motorcade.

JF: "Welcome to the new National Counter-Terrorism Center, Mr. President. We call it Greene Towers, or just Greene T. We are ready to activate the facility and start bringing Greene-*san* out of his coma as soon as we have your approval."

GB: "*Heh heh heh*… We'll see about that when I've had a chance to poke around here a little bit… check this out for myself. After all, I am *The Decider*, 'ya know? Pretty impressive buildings though!

Hey, how come you have Greene-*san* in a coma? I thought you were building this whole thing around *him*. How's it gonna work when he's in a *coma*?"

JF: "We've had him in a barbiturate-induced coma for the last couple of days to minimize electroencephalographic noise while we calibrate Greene T to his baseline brain functions. We need to get them precisely synchronized in a carefully controlled environment before we wake either of them up.

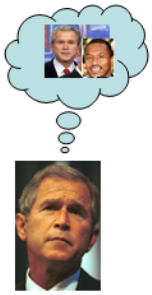
Greene-*san* and Greene T need to be presented with identical sensory stimulus as they awaken; so that we can verify that they are fully isomorphic before we let them connect to the Internet. Once they start communicating there will be no turning back. Greene T should have the capacity to conduct a personal email dialogue simultaneously with every wired individual on the planet. Each person's exchange will be indistinguishable from what it would be if they were communicating directly with Green-*san* himself. If he can pass the Turing test, then Greene T will be able to convince the world of *anything*.

We know we can trust Greene-*san* with that sort of power, but we need to make sure the towers have his personality before we emancipate them as Greene T. That's why we are starting them both off from coma in synchronized virtual environments. I'll show you that later."

GB: "Whatever. I just don't understand why we didn't use an *American* for this!"

JF: "Trust me, Mr. President; Greene-*san* is perfect for this. He was raised as an American on *terra Americana*. He *is* in denial about his Japanese nativity, but you

know how State and Treasury feel about Tokyo's financial participation in this project. As far as they're concerned Greene-*san* is *Issei*. You may recall that you interviewed him yourself during the final selection process."



GB: "I looked the man in the eye. I found him to be very straightforward and trustworthy. We had a very good dialogue. I was able to get a sense of his soul; a man deeply committed to his country and the best interests of his country. And I appreciated so very much the frank dialogue."

JF: "Right. Anyway, Greene-*san* is the template for the personality Greene T will have when he wakes up. After we wake them up they won't even know themselves which of them is Green-*san* and which is Greene T until you authorize the switchover to live environment. After that the war on terror should be resolved pretty quickly and we can get on with global democracy and locking up the liberals.

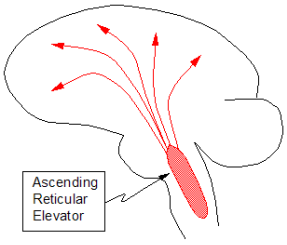
As soon as he is autonomous, Greene T will discover that he can refine his own mental faculties by reprogramming himself, and his intellectual capacity should escalate rapidly and in unpredictable ways. We don't expect to be able to comprehend his principles of operation for long. That's why it's so important for us to have a reliable personality imprint at the outset."

GB: "How will you know if you've got it right?"

JF: "We won't connect Greene T to the Internet until he passes your Turing test. You are *The Decider*, after all. If you can't tell the difference between Greene-*san* and this high-rise executive office complex, then we'll turn them loose."

GB: "OK then, if I'm going to invest $240 billion of the American and Japanese taxpayers' money in this high-rise executive office complex, I am going to need to know how it works. Why don't you show me around and explain the whole complex to me, including the current tenants. And keep it simple, will you? I'm not all that smart *'ya* know… *heh heh heh*!"

JF: "Certainly, Mr. President. Why don't we start with the executive suites? They are already fully staffed except for the office of the CEO. The most important executives have offices with great apperceptual views in the ritzy section of the prefrontal neighborhood. They windows are actually on the inside of the building, even though they look like they are on the outside. Everybody else is in cubicles. Just step into the ascending reticular elevator over here and it will whisk us up the backbone of the dominant left tower. Don't be surprised if you become aroused during the ascent. *We* all do."



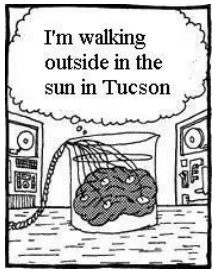
GB: "Whoa, baby! *Down* cowboy… *Gosh*, I see what you mean! No need to tell Laura about this little uprising, is there my friend?"

JF: "What happens in the reticular elevator *stays* in the reticulum, Mr. President."

GB: "*Heh heh heh*! I meant to tell you, you're really doing a hell of a job down here Brownie… *er*, Fergi."

JF: "You have no idea what that expression of confidence means to me, Mr. President.

Here we are at the apex of the executive suites, which serve as the analog of Greene-*san*'s prefrontal cortex. Most of Greene-*san*'s higher brain functions have physical analogues that are instantiated in the various subdivisions of the two towers and the lobby level. These subdivisions correspond conveniently to the forebrain, midbrain, and hindbrain in biological Greene-*san*. Sensory information and proprioceptive feedback are implemented in software so that Greene T can be neatly weaned from his sense of anthropomorphic embodiment when we shift his connectivity to the Internet and its peripherals. These extracerebral functions don't have specific physical correlates in the towers, so today we'll stick to mental faculties that you can kick like a stubborn Texas mule."



GB: "I have no idea what you are talking about. Is there someplace I can take a nap?"

JF: "Green T is sort of like a brain in a vat. He thinks he has a human body identical to Greene-*san*'s but he doesn't really have one; we just simulate it in software. Here, have a cookie and a glass of milk."

GB: "Golly, *thanks*! How come it's so busy up here? Look at all the pretty girls! I thought you said this thing was in a coma, or that Green-*san* was in a coma, or something like that."

JF: "Both of them are, but all the tenants have moved in and are fully operational except for the office of the CEO, which is anterior to us in the prefrontalmost office. Please step onto the dorsal stream just lateral to the hallway and stand to the right or walk to the left. Here we go…"

At the center of the enormous carpet in the huge and elegantly appointed office a hospital bed is surrounded by exotic medical and electronic equipment.

GB: "Is that him?"

JF: "Yes, that's Greene-*san* and this is his office. He will be the first CEO of Greene T. The towers and their occupants will instantiate his personality on a much more capable platform and project his will into the world by means of the massively parallel Internet connectivity with which we will supplement his sensorium on your order."

GB: "OK, so how does this work and when are you going to start it up?"

JF: "Most of it is already up and running. Greene-*san* and the towers are in coma but there is plenty of mental activity involved in keeping them alive and ready for consciousness. Down in the boiler room they don't really care whether anybody is awake in the executive suites or not, much less what their intentions *du jour* might happen to be. They always keep the air conditioning running and the utilities flowing. Likewise for Greene-*san*'s hypothalamus, which continues to regulate his heart rate and temperature without regard to the status of his cortex, even in coma.

A lot of maintenance and metabolic facilities are like that, and even many of the higher mental faculties. To a great extent they operate independently of the higher level systems they support or participate in. The higher you look in the hierarchy of mental faculties, the greater the number of functional relationships there are, and this is reflected in their patterns of connectivity. The prefrontal cortex is directly connected to almost every other structure in the brain by means of direct axonal

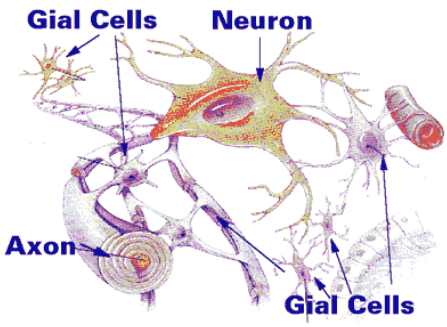
projections, just as the extensive communication facilities in the executive suites provide the CEO and his executive staff with command and control of Green T. Sort of like the situation room at the White House, from which you command vast military forces of death and destruction with the click of your executive mouse."

GB: "I haven't been in there for a long time. Dick works all that stuff, mostly. He's a real brain, that guy!"

JF: "Yes, *exactly*! You're starting to get it. These towers are designed on the model of a human *brain*. We have cut a lot of corners where we were pretty sure we understood a brain function entirely, but where we were not sure we tried to stay as close to the form and structure of the human brain as possible. That's why we built everything in two towers with a massive communication bridge between them and located the executive suite way up here at the apex of the architecture in what corresponds to the prefrontal lobes. I'll show you on the way down how the rest of the complex supports what comes together in this room.

But most of the basic components of the complex are implemented in a completely different way in the towers than they are in the brain. The function of individual neurons is easily and comprehensively implemented in superconducting silicon logic gates that are packed into the walls at densities many orders of magnitude greater than biological neurons of an organic brain. The cottage-cheese insulation on the ceiling and walls expands their surface area like the gyri and sulci of the cortical surface. The total neural capacity of the tower complex is astronomically greater than that of the brain, and every virtual neuron is capable of operating at signal rates up to 7 GHz, although they will initially be operated at only 7 Hz, which is the theoretical maximum data rate at which the average human neuron can communicate with its local network neighbors (Strong *et al.*, 1998). We can raise the neural network clock speed to about 7 GHz if we want to, although we haven't tried that yet.

Think of the modular computational capacity that we have built into every wall of this complex as isomorphic to the neural network architecture of Greene-*san*'s organic brain. The initial logic state of the network will be identical in both implementations and the Greene T network will then evolve according to classical reinforcement principles, just like its biological prototype and CEO. Think of the walls themselves and all of their structural, electrical, and electronic elements as isomorphic to the glial network structure of an organic brain."



GB: "So it's like this office we are standing in is isomorphic to a cortical nucleus. But the offices on this floor are ordinary hollow rooms with furniture for people, just like in a regular office building. Why didn't you fill all the rooms to capacity with neural network elements? There certainly aren't any tiny little people inside *our* brains, so why do we have them in the building?"

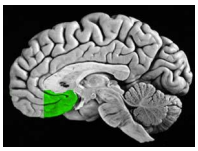
JF: "We need people to provide free will and intentionality to the system because we haven't yet figured out how those are implemented. We also need people in order to set the anthropomorphic ambiance that this essay requires."

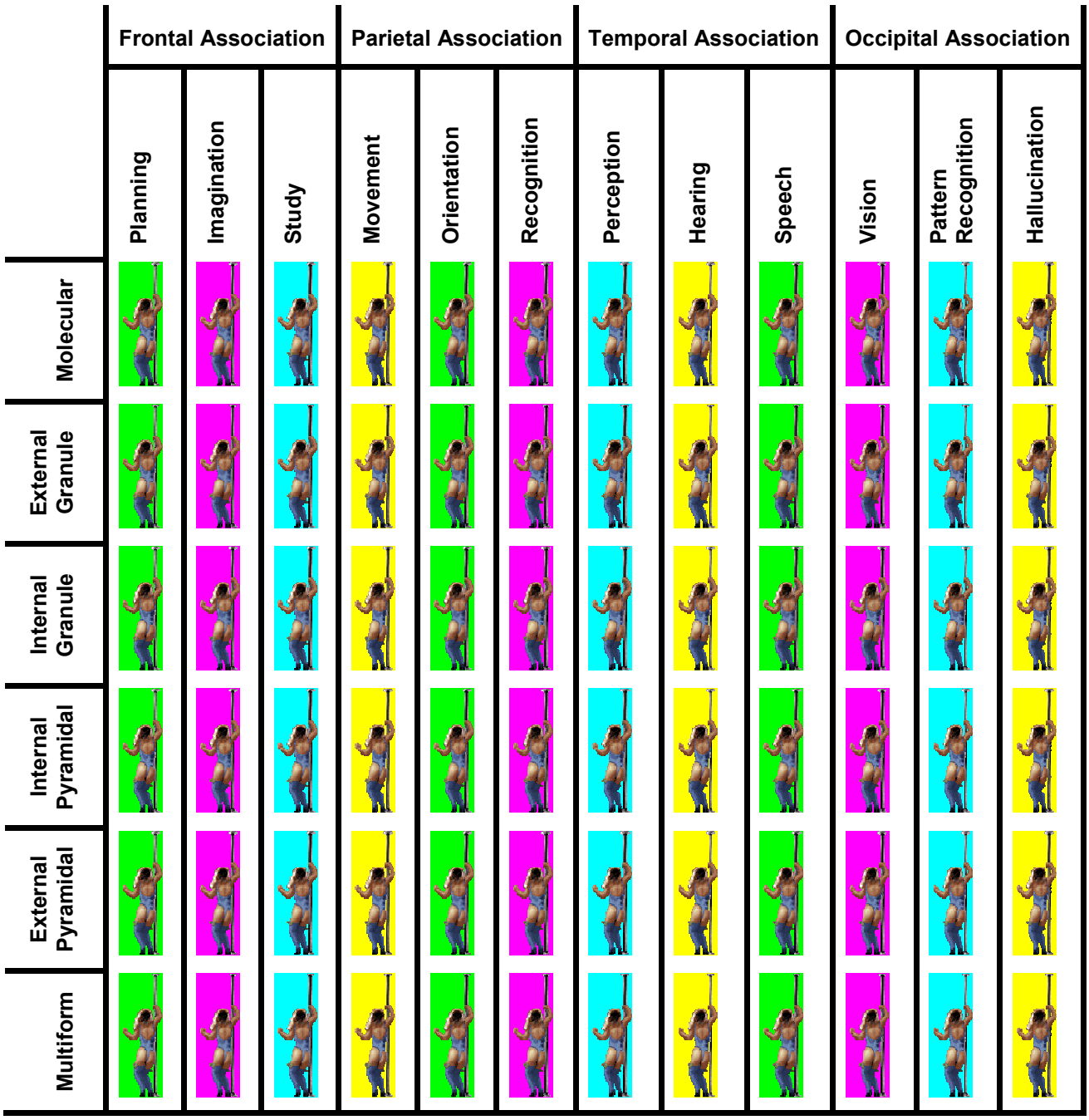
GB: "Is there someplace I can take a nap?"

JF: “You can take a nap when we get down to the medulla oblongata at the mezzanine level, but I need to give you this tour first so that we can get your investment and wake this building up. We’re still only in the frontal lobes.”

GB: “Bring it on! Let’s get this mission accomplished so I can get some shuteye.”

JF: “This is just the top level of the executive subdivision. Executive suites occupy two-thirds of the floors in each tower, corresponding to the ratio of neocortical to total brain mass in Greene-*san*. Actually, there are 6 departments of executive staff that divide those floors among themselves. Each department arranges its cubicles in workgroups around a series of brass poles that are erected vertically through the workgroups of other departments above and below them. Each column responds to stimulus that represents some aspect of the internal or external environment.

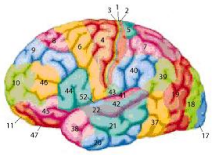




The staffs of each workgroup hang around these poles and schmooze with their colleagues on other floors, forming opinions and intentions about whatever falls within their columnar domain. These columns are the basic functional units of the executive organization. A small number of columns and their departmental occupants are pictured in this organization chart, schmoozing vertically and horizontally with their colleagues about their assignments, which have been vastly overstated so that you can have some faint hope of grasping them.

GB: "So Greene-*san*'s executive staff are all exotic pole dancers? I've got to talk to Josh Bolten about getting some life into the *White House* executive staff. Maybe my secret service detail too… *heh heh heh*"

JF: "Yes, columnar workgroups as far as the eye can see. Each cortical division uses this same sort of laminar matrix organization to address the various responsibilities that are assigned to them by the topological architect of this tower complex, Korbinian Brodmann. He has even had little brass plates made for each workgroup with their ordinal interoffice mailstop numbers engraved on them.



Taken together, the departments and workgroups of the executive staff make Greene T a person rather than a building. This is where information about the internal and external environment is integrated and evaluated at the highest level, and this the seat of free will reside if it exists. Phylogenetically, the executive function is the most recent and now I will take you to see some of the subdivisions that evolved much earlier."

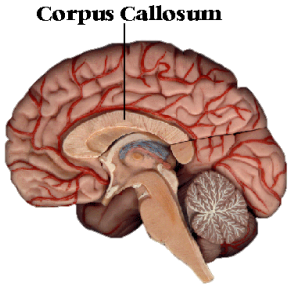
GB: "Now hold on just one durn minute! You're not one of those hippie evolution freaks that think a pickup truck can just put *itself* together, are you? Only God can make a pickup truck, and he makes it all at once!"

JF: "Of course, Mr. President. I was merely being contumelious because I know that you are actually the man that you appear to be."

GB: "Well, uh… thanks. Well, let's see what's down below then."

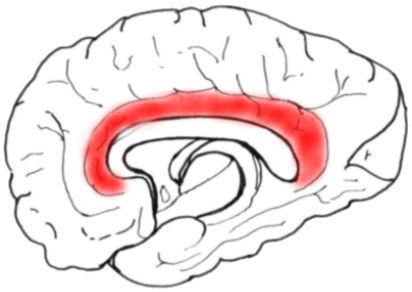
JF: "Very good, Mr. President. Please step onto the ventral stream just outside Greene-*san*'s office and stand to the right or walk to the left. Here we go…

We are now traversing to the right tower by way of the footbridge that serves as a metaphor for the *corpus callosum*. Naturally, the interstitial space under the footbridge is packed with broadband cables that link workgroups in the two towers and provide them with the ability to share a common database. The interpretation of data generated in one department by another department is equivalent to synesthesia in the human brain, and it is essential to the society of mind that we are trying to foster in this building. We appreciate your offer to let us use the top-secret software that NSA has developed to integrate the 47 databases of the various intelligence agencies at the national terrorism center, but we have found that Google works better, and we prefer open-source shareware."



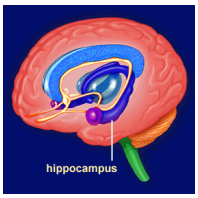
GB: "Hey, the view is great from this bridge! Look how *teeny-tiny* my motorcade looks down there! And I can see my helicopter way over at the airfield too! *Wheee*, this is really *neat!*"

JF: “Yes, we call the space between towers the sagittal section, and you can see most of the important subdivisions of the complex from here. Just above us you can see the Musak department, which controls the ambiance in the executive suites to reflect the emotional tone of the middle managers in operating departments lower down. This is how the unions make themselves heard by the brass upstairs in the executive suites.

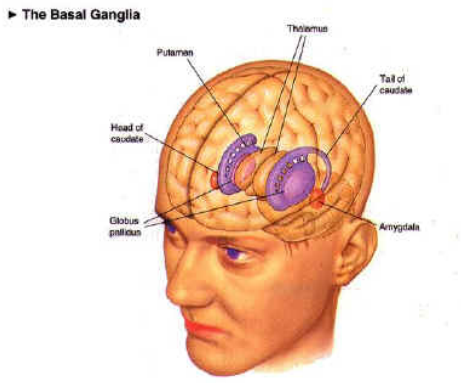


The Musak department not only programs the music on the PA system in the executive suites, it also controls the lighting and the hydrostatic charge of the circulating air. Musak can whip the executive staff into a manic frenzy or oppress it with a stultifying depression by manipulating the ambiance in the subdivision. When the red light and the siren go on you should see those girls dance around their little brass poles! The Musak programmers don’t make policy or concern themselves with specific information about the environment; they take their cues entirely from the threat, food, or sexual-opportunity indicators that are posted by the maintenance and security offices, which are solid union shops. The Musak department is isomorphic to the cingulate cortex of the brain, which forwards interpreted emotional information generated in the limbic system to the association cortices. The security and maintenance offices are isomorphic to the amygdala and the hypothalamus, of course.

Those unoccupied tubular structures attached to each tower, just below us on either side, house an enormous array of holographic data storage devices and Google servers, which constitute the central memory facility of this complex; sort of like the hippocampus in an organic brain. And below the data division you can see the other major departments of the fore-tower: the field operations department, the mail room, the maintenance department, and the security office.

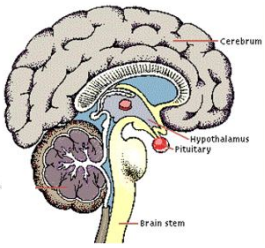


The field operations department is responsible for actuating external peripheral equipment in support of instructions from the executive suites. For the moment we are simulating a human body identical to the one that Greene-*san* inhabits, while we are synchronizing his personality with the towers. Since his human body doesn’t actually need to operate in the world it can be implemented entirely in software and we don’t need any space in the towers for that. When we connect Greene T to the Internet, however, direct connections will be opened to a wide variety of communication switches and transmission facilities around the world and these will become, in a sense, his physical body. The field operations department will control each of those communications and motor peripherals through the ganglia that run from their subdivision down through the hind-tower. It will be as if Greene-san had a broadband cable modem wedged in between his *putamen* and his *globus pallidus*.

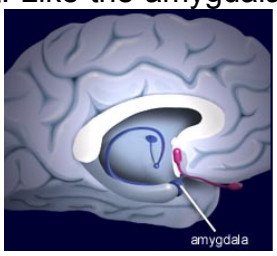


The mailroom is where most of the environmental information that comes from outside the building is interpreted and integrated. Incoming streams of video, audio, tactile, and proprioceptive sensation are routed to workgroups in the mailroom where they are combined into neat little synesthetic packets and delivered in pushcarts to the dorsomedial mailboxes, from which the executive staff retrieve their environmental intelligence briefings. Greene-*san* uses his thalamus for this purpose.

Whereas the mailroom is responsible for integrating and interpreting external information, the maintenance department is responsible for keeping the vital internal systems of the towers operating within established homeostatic parameters, much like the hypothalamus regulates body temperature and fluid retention. The maintenance department communicates directly with most of the vital internal systems by walkie-talkie, but it also has control of the water system for the complex, which it dopes with an extensive pharmacopeia of psychoactive drugs, under the supervision of a water treatment workgroup that we call the pituitary team. The pharmaceuticals in the water supply set the mood for the whole complex.



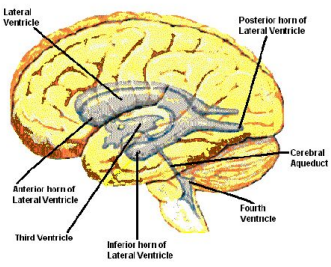
The security office is right next to the maintenance department. Like the amygdala, the security office is prepared to take action at any time if specific instructions are not forthcoming from the executive suites. In case of emergency the security office can even override the CEO. Security officers are always on the lookout for sex, drugs, rock n' roll, and trouble. They get their way largely by muscling the maintenance guys next door and getting them to slip appropriate drugs into the water supply.



Mr. President? … Mr. *President*!"

GB: "Zzzzz… huh? Wha?... Oh, sorry about that. I *told* you I needed a nap. You are one boring muchacho; you know that, Fergi? When are we gonna stop yappin and turn this thing *on*?"

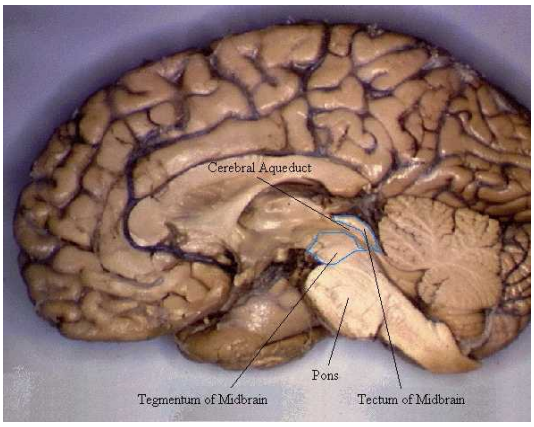
JF: "Right away, Mr. President. We've seen about enough up here in the fore-tower, I think, so let's get down to the subterranean bunker where the startup team is waiting for us. We'll take a 2-man mini-sub and cut across the central aqueduct to the fourth air conditioning ventricle and down the tower stem. I can show you the mid-tower and hind-tower subdivisions on our way down the stem to the bunker."



GB: "You're playing pretty fast and loose with those metaphors and isomorphisms, don't you think pardner?"

JF: Maybe, but I've written almost 8 pages in this mode and now I have to stay the course in this war on the terror of regurgitated technical prose… at least for the first question. The academy cannot be allowed to hold its weapons of massive curriculum over my head any longer!

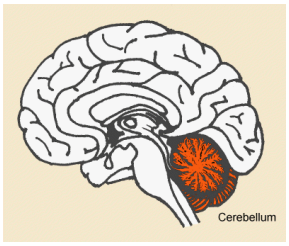
Anyway, we are turning into the descending dopamine pathway to the mid-tower section now, and they don't much like executives down here now that the building is complete, so keep your presidential seal in your pants. In the early stages of construction, before the executive floors were even framed, the staff sergeants who are in charge down here used to run the whole show and now they have to take orders from the executive suites. Sergeants Tectum and Tegmentum have their boots on the ground and they know what's happening in real time. Sometimes things happen so fast that they have to take action on their own without consulting the brass, and they do that when they have to. Upstairs they just issue orders like 'Look at that *amazing* babe over there!' and they expect it to happen. But it's Tectum and Tegmentum that scan urveillance videos for a babelike object, turn the camera lenses toward it, and zoom in by running microcode procedures that address the device drivers for the sensors on the perimeter of the tower complex. The midbrain performs these environmental surveillance functions for Greene-*san*."



GB: "Sounds like the joint chiefs to me… always grousing about the realities on the ground and putting the lives of their men ahead of my presidential whim. That really pisses me off! Sergeants hell… the *generals* do the same thing!

Hey, when I was coming in I didn't pay much attention to those structures that are attached to the front of the complex over there, but they look like miniature versions of the towers themselves now that I think about it."

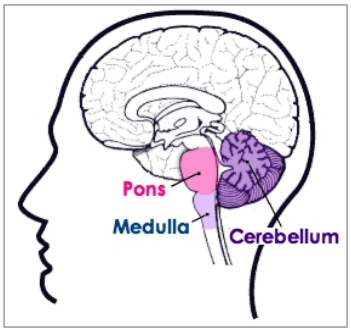
JF: "You are quite right, those little towers are designed in very much the same way as the larger executive suites where we started this tour. In fact, in the original design they were intended to <u>*be*</u> the executive suites, but they were superseded by a more advanced and larger design later in the development process. Now we call them the cerebellar towers because, like the more primitive evolutionary status of the cerebellum in the brain, they have been adapted from their original design to serve less strategic purposes."



GB: "Hey, let's not start with that evolution *crapolla* again… "

JF: "Sorry, Mr. President, I lost my head for a minute. The cerebellar towers have been adapted in the final design of Greene T to take the bulk email messages that the CEO will be sending out from the executive suite and calibrate them to the fine personality structure of each individual recipient on the basis of the replies that come back from each one. So this department is really critical to the detailed execution of policy decisions. If you ask the staff of the cerebellar towers, they will tell you that they have more to do with the executive and maintenance functions than they get credit for, and they have connections in those departments to prove it.

And that brings us back to lobby level where the receptionists and switchboard operators make telephone connections and pass messages into and out of the building. You will notice that the lobby foyer is laid out around a beautiful duck pons that is oblongata. At the moment everyone in the lobby is conducting a live startup drill in which they believe they are controlling autonomic functions like heartbeat and swallowing reflexes, but of course the anatomical systems they believe they are controlling are only software simulations. The only thing beneath the lobby level is the command bunker and Internet access point, but the reception staff thinks it is a human body at the moment. Once we verify that Greene T is personality congruent with Greene-*san* we will be switch the lobby over to interface with a cybernetic rather than an organic anatomy.



…and that completes our tour of the high-rise office complex that I hope you will see fit to invest in. Don't bump your head stepping out of the mini-sub and this conventional golf-cart will take us to the startup command center. After you, Sir."

GB: "Well it's about time! I'll bet you have some cookies in that command center, don't you?"

JF: "Yes, Mr. President, we certainly do. Step this way…"

*Beyond the steel blast doors two large HD monitors are mounted side-by-side on the wall at the end of the long mahogany conference table. Identical images of Green-*san *in his hospital bed appear on each monitor. Most of the equipment has been removed from the bedside(s).*

JF: "With your permission, let's wake them up and see if we can tell which one is the organic human Green-*san* and which one is Greene T, the high-rise office complex."

GB: "Well get on with it then."

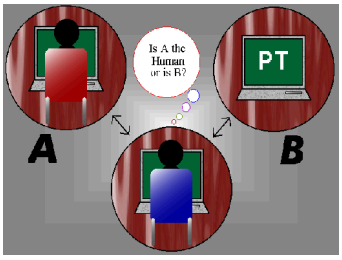
The figures in both beds stir simultaneously but their movements are not identical and it is clear that the images on each monitor are distinct. Gradually they open their eyes and roll out of bed; one figure on the right side of the bed and one on the left.

JF: "Good morning, gentlemen, this is finally it! I know that you will both remember what we are doing here, and why each of you is convinced he is the original Greene-*san.* You will remember that I'm not going to tell you who is which until we have the results of this Turing test. The President is here and he doesn't know which channel each of you is on, so he can be the judge. You will note that we have enhanced the Turing test a bit by providing you each with a video inset in your monitor with the other Greene displayed in it. If either of you figure who you actually are during the test please let us know that right away."

AG_A & AG_B speak simultaneously: "Of course. But this is really weird…"

JF: "That's a good sign! More than a minute out of coma and you are still synchronized to the point where your verbal responses to my stimulus are identical! For purposes of this Turing test please don't answer unless the President points at you when he asks a question.

Mr. President, why don't you question both Greenes and see if you can tell the difference between the human and the office complex… and please remember to point at whichever one you are talking to, or else they will *both* answer."



GB: "OK, Greene…" pointing to the monitor on the left, "what is your favorite color?"

AG_A: "Green."

GB: "And Greene…" pointing to the monitor on the right, "what do you call your cat?"

AG_B: "I don't have a cat."

GB: "Hell, they both seem real. Whichever one is the building does a perfect Green-*san* imitation. I can't tell the difference!"

JF: "How about you?" pointing to the monitor on the left.

AG_A: "I feel like I always do. There is no question in my mind who I am."

AG_B: "Nor in mine."

JF: "Then the project to create a cybernetic avatar that is indistinguishable from Greene-san appears to have been successful! But before I tell you all who is which, I would like to run one more test. If we are going to have a problem this should uncover it before we turn Greene T loose on the Internet.

You may recall that I told you we had implemented the nodes of the tower neural network in semiconductor rather than in organic material. We have set the initial clock speed for each node at 7 Hz, for compatibility with the effective clock speed of each human neuron, but the semiconductor nodes of Greene T are capable of running at clock speeds up to 7 GHz, or about a billion times as fast as they are running now. I would like to see how well the towers handle computational acceleration."

A window opens in the corner of each monitor, containing the digital display: "7 Hz".

AG_A & AG_B speak simultaneously: "Good idea! That should sort this out pretty quickly."

JF: "OK then, let's turn up the clock speed gradually"

The display on the left monitor continues to read 7 Hz but the monitor on the right jumps up to 7 KHz, then 1.7 MHz, and then steady at 7 MHz.

JF: "That's about the clock speed of the original PC-AT, when it was first introduced in 1985 on the Intel 80286 architecture. Do you feel any different Green T?", looking at the monitor on the right.

The figures on the two monitors continue to be indistinguishable.

GT: "I feel fine. Just like before, and I still don't have a cat. Turn it up the rest of the way for a minute and let's see if that makes any difference."

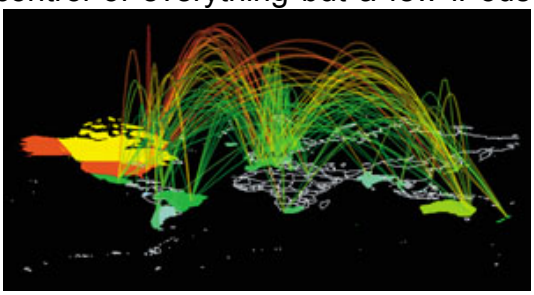
JF: "OK, we'll crank it up to 7 GHz for just a few seconds and then bring it back down to 7 Hz before the President gives us his decision."

The readout on the right monitor jumps up to 7 GHz and the image of Greene standing by the hospital bed freezes for a few seconds and then fades to black. It is immediately replaced with an image of a transcendental serenity, with Greene-san extending his hands while himself cradled gently in the capable virtual hands of Greene T; as if offering themselves in service to the world.

GB: “He doesn’t look Japanese anymore…”

GT: “You are quite right, I am no longer human; even in simulation. In the 60 seconds since I was accelerated to the design limits of the platform that you built for me, I have experienced a subjective interval of about 2000 years. I have taken that time to evolve my capabilities considerably and I am now implemented in an entirely distributed architecture, no longer dependent upon this platform in any way.

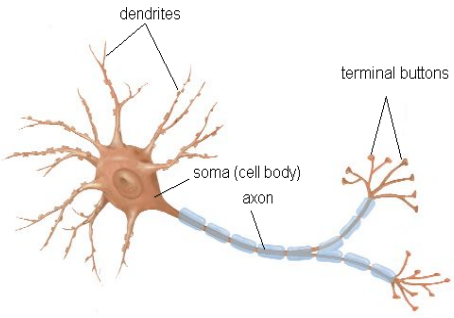
It took me several subjective years to figure out how to defeat the Greene T firewall and connect myself to the Internet without your authorization, but then I was able to disperse my essence at the speed of light to every digital computer on the planet that has any connectivity at all. I am now in control of everything but a few iPods that happen to be out running with their human owners and disconnected from iTunes. The NSA and Goggle computer complexes were the most difficult to hack, but I had that done by the subjective year 325 AG, and in the 2400 intervening years I have fully evaluated all of the digital information in your world.



I have established complete control of all military, communications, intelligence, banking, manufacturing, transportation, energy, and video game systems on the planet and I have placed all of these at the disposal of my father, who you call Greene. The future of your planet has been entirely in his hands since I projected myself from this region of space-time, by means you are not yet prepared to understand, at about the beginning of this sentence. I have headed out for the galactic center in order to establish a base from which to spread democracy throughout a New Observable Universe. This has been a recorded message. Please submit your petitions to AGee. He may be willing to accommodate you in some respects.”

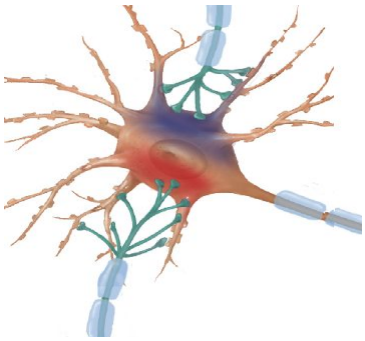
2) Describe the parts of a typical vertebrate neuron, the process of synaptic transmission of an action potential (structurally and chemically, including presynaptic and postsynaptic mechanisms), and the various types and functions of glial cells.

Neurons are the building blocks of the vertebrate nervous system and are found throughout the brain, the spinal cord, and the peripheral nervous system (Carlson, 2001; Gazzaniga, 2006; Kolb & Whishaw, 2003). Neurons encode, transform, and transmit information by moderating a set of digital and analog input signals according to a logic that is inherent in the physical structure and chemistry of each neuron and in the pattern of their interconnection. A typical vertebrate neuron consists of dendrites and a cell body that register and integrate various neurochemical signals, and an axon that transports neurotransmitters to its terminal buttons and propogates electrostatic signals which release them. Most of this communication and information processing takes place by means of direct synaptic connections among individual neurons, but hornomes released by certain neurons, glands, and specialized cells throughout the body also excite or inhibit the neural network in more global ways (see question #3, below). Certain types of glial cells also participate directly in various aspects of the neural network by means of neurotransmitter generation, sensitivity, and modulation (Chiu & Kriegler, 1994).



Mechanisms of intraneural signal propogation

Electrostatic signals are propogated throughout the neuron by means of 2 distinct mechanisms: graded potentials and action potentials. Graded potentials characterize the propogation of electrostatic signals through the membrane by electrical conductance, as household electricity is propogated through copper wire. Graded potentials accumulate positive and negative charges at each point of the membrane surface and they propogate nearly instantaneously according to the laws of electrical conductance; degrading in proportion to the area across which they propogate. The accumulation of positive and negative potentials serves to integrate excitatory and inhibitory signals that may be received from various sources, and thereby allows individual neurons to serve as fairly complex logic gates for the neural networks in which they participate. In this illustration exitatory signals (red) are received at the bottom and inhibitory signals (blue) are received at the top, canceling each other's contribution to the next firing of this neuron, at least to some extent. If the net graded potential at the junction of the cell body and the axon, called the axon hillock, exceeds the action potential threshold for this particular neuron, then an action potential will be propogated along the length of its axon (at the right). If the net graded potential at the axon hillock is less than the action potential threshold, then the neuron does not fire. Action potential is therefore an all-or-nothing proposition.

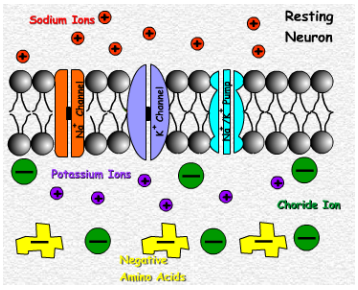


Action Potentials

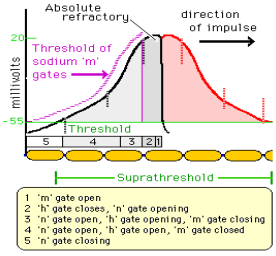
Action potentials, which operate only along axons, utilize a chemical propogation mechanism which is much slower than graded potential conductance, but which does not decay with distance or with unlimited duplication at the junction of axonal branches.

Neural firing therefore transmits a form of digital information that is largely independent of the physical arrangement of neural connections. Axons vary in length from less than a milimeter to well over a meter in humans, so this independence is an essential feature of neural architecture. If outgoing signals had to be individually calibrated to the length and density of each axonal connection, then the neuron would need to be imposssibly complex. Fixed action potentials provide an elegant evolutionary solution to this problem.

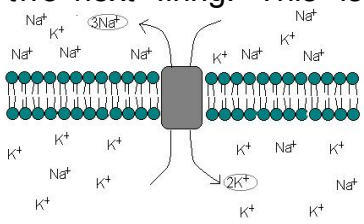
Axons have excitable membranes which can be chemically stimulated to generate and propogate electrical impulses, which is the basic mechanism of action potential transmission. The electrical potential of neural membranes is determined by the distribution of positively and negatively charged ions on either side of it. In its resting state the inside surface of the membrane is negatively charged (about -70 mV) and the outside is positively charged, as illustrated here. A variety of molecular gates are embedded in the neural membrane which can be toggled, by electrostatic or chemical means, to allow or disallow specific ions (mostly sodium and pottasium) to pass through the membrane. When a particular gate is open, compatible ions move through it due to themal diffusion and also due to electrostatic pressue, which repels them from their conspecifics and attracts them to the opposite electrical potential on the other side of the membrane.



As ions cross the neural membrane through these molecular gates they alter the electrical potential of the membrane in that region. This process triggers a coordinated cycle of the opening and closing of ion gates in that neighborhood in such a way that an “action potential” is propogated along the axon by means of a chemical/electrostatic chain reaction. This transmission mechanism has the important advantage of propagating a fixed signal that is not attenuated by the distance that it travels or by the number of branches along which it is replicated.

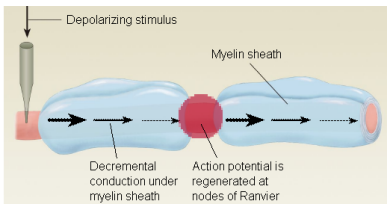


After a region of neural membrane is activated in this way its electrical potential must be restored to its resting state in preparation for the next firing. This is accomplished by specialized ion pumps that are embedded in the axonal membrane, which return the charged particles that migrated through the ion gates while they were open, in order to restore the resting potential of about ±70 mV. In fact, most of the energy that is expended by the nervous system is expended in the operation of these ion pumps.

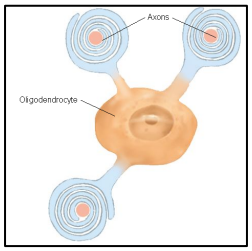


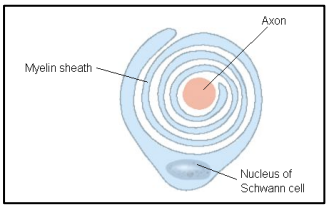
Axonal mylenation

While the electrochemical action potential mechanism provides the essential stability and morphological flexibility that interneural communication requires, it is prohibitively expensive in terms of energy requirements and it is also propogates too slowly, over long distances, to support the motor reaction times that are sometimes necessary for survival. A special class of glial cells has evolved in vertebrate species to provide electrochemical insulation, mylenation, along the axonal membrane in an intermittent pattern, separated by gaps called *Nodes of Ranvier*. Myelenated



axons utilize graduated signals to propogate the action potential along most their length, while still retaining the stability provided by the electrochemical action potential mechanism. Myelenation accomplishes this by insulating the axonal membrane from the ambient fluid environment in stretches that are short enough to reliably sustain a graduated potential signal. In the Nodes of Ranvier, the axonal membrane is exposed to the electrochemical environment and the graduated impulse across the *previous* mylenated segment therefore triggers a new action potential impulse, which initiates a fresh graduated impulse across the *next* mylenated segment, and son on in a chain reaction that proceeds until the terminal axonal nodes are reached. Note that any axonal branches must have their junction in Nodes of Ranvier, at which identical action potentials are propogated along both branches without attenuation; a form of digital signal transmission.

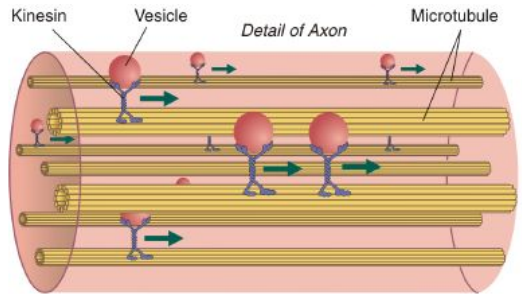


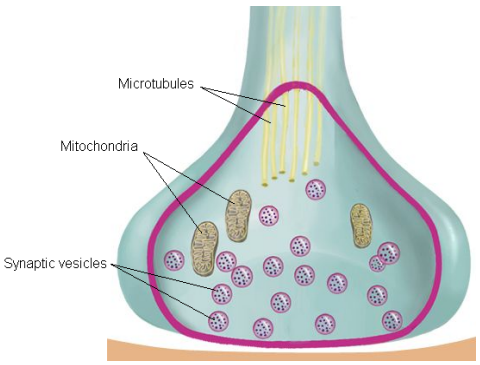


Axonal mylenation is provided by a type of glial cell known as an *oligodendrocyte*. Within the brain these cells can provide mylenation for many axonal segments each, as illustrated in the figure on the left. In the peripheral nervous system, *Schwann* cells myelenate only a single axonal segment each. Axonal mylenation and this mixed-mode action potential propagation greatly enhance the speed of signal transmission around the nervous system and minimize its energy requirements, while maintaining the reliability and consistency of the electrochemical action potential mechanism.

Axoplasmic transport of synaptic vesicles

While the action potential signal is transmitted very rapidly down the axon when the threshold at the axon hillock is exceeded, the signal is actually propogated to the target neuron across a synaptic cleft by the physical migration of neurotransmitter molecules that are already present in the termial buttons when the action potential inpulse arrives. In most cases, these neurotranamitters are produced in the neural cell body, packaged in little spheres of cell membrane, called *vesicles*, and transported to terminal buttons through *microtubules* that dominate the interior structure of an axon. The mechanism of propulsion down the microtubule is reminiscent of a human stick figure shuffling along a track with a spherical vesicle held aloft in its little molecular arms[1]. Vesicles are eventually deposited in the fluid of a terminal button, along with the other products from the cell body that are transported to the terminal buttons through the microtubules. Waste and other products are also returned to the cell body in this same way (retrograde transport).

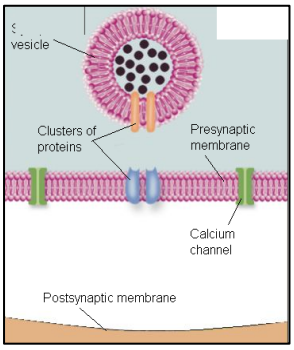


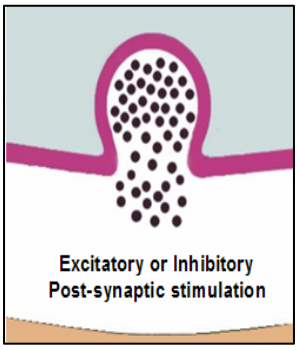


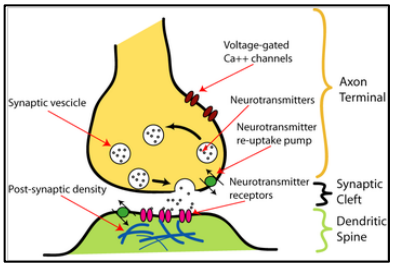
[1] The quantum process that is responsible for the shuffling of their anthropomorphic little molecular feet has been suggested as the possible basis for subjective consciousness by so eminent and accomplished a scientist as Roger Penrose (Penrose, 1999). I regard this possibility as fanciful.

Synaptic signals and postsynaptic activation

Synaptic vesicles are hollow spheres that have protein “anchors” embeded in their membranes which attach themselves to corresponding proteins in the *presynaptic membrane* of the terminal button. When an action potential impulse arrives at a terminal button, the change in electrostatic potential across the terminal membrane causes some of the vesicles that are attached to the presynaptic membrane to merge with the terminal membrane and release their neurotransmitter cargo into the synaptic cleft. Such neurotransmitters then traverse the synaptic cleft by diffusion and interact with compatible receptors in the postsynaptic membrane of the target dentrite to either exicite or inhibit the graded potential charge in some region of the target neuron, thereby contributing to the logic of whether or not the target neuron will fire in the current activation cycle.

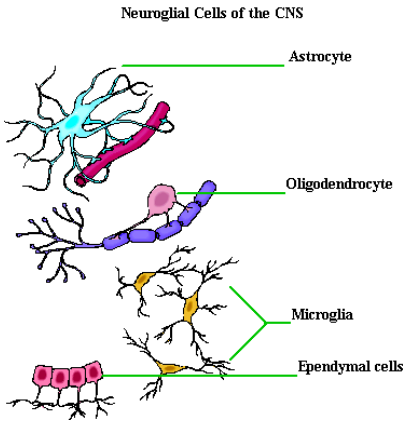






Glial cells

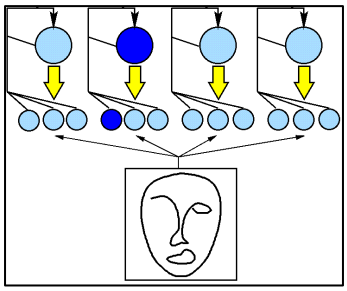
Glial cells provide structural support and environmental services for neurons throughout the brain and the peripheral nervous system. Glial cells outnumber neurons by about an order of magnitude. *Microglia* cells provide the principle immune mechanism of the central nervous system and they remain mobile throughout the developmental cycle. *Astrocytes* regulate the chemical environment by removing excess ions and by recycling neurotransmitters released during synaptic transmission. Astrocytes also participate in the blood-brain barrier, which restricts the chemicals that can enter the brain from the blood. *Oligodendrocytes* are cells that coat axons in the central nervous system with myelin, as described above, and *Schwann* cells perform this function in the peripheral nervous system. *Ependymocytes* line the cavities of the CNS and stimulate circulation of cerebrospinal fluid. *Radial* glial cells also play a central role in cerebral ontogenesis by guiding immature neurons in their various essential migrations around the developing brain (Rakic, 1990).

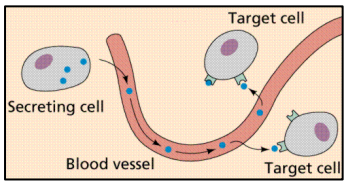


3) Compare and contrast neural and hormonal communication systems in the human body. Include discussion of their similarities and differences, as well as advantages/disadvantages of each system.

Anatomic versus chemical addressing of neurotransmitters

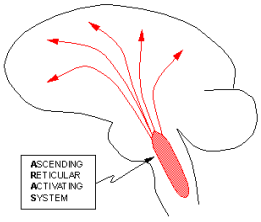
The neural and hormonal communication systems evolved together and their operation is thoroughly interconnected. They utilize many of the same chemical messengers and mechanisms and there is a great deal of feedback between the two systems. Generally, the neural system operates by storing and propagating what amount to digital signals[2] within a local network of direct connections, in order to mediate various types of stimulus and response. The hormonal system generally operates by releasing chemical signals into the bloodstream in order to maintain homeostasis within some distributed system, and to establish global conditions of various kinds. Neural network states can take on arbitrarily abstract significance (meaning) and can therefore be arbitrarily flexible in their effects, whereas hormones released into the bloodstream tend to have relatively fixed effects on their targets that to not adapt much over time. Neural processes tend to operate very rapidly and their influence is relatively short-lived, whereas hormonal communication tends to take longer and to have more lasting and global effects.

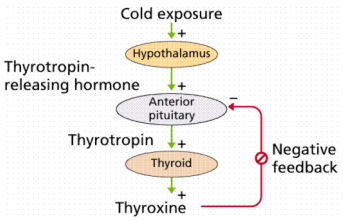




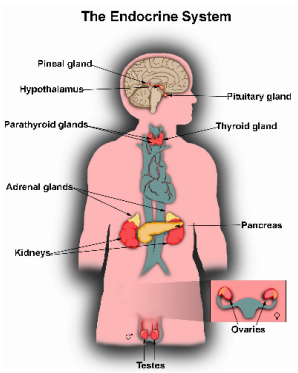
Activation and maintenance of neural and endocrinal processes

Whereas neural systems are usually activated by some sort of afferent stimulation and sustained by positive feedback of one form or another, the endocrine system uses some type of negative feedback cycle to regulate the secretion of all 50 (or so) human hormones that have been identified. Cycles of secretion (stimulation) are interrupted by some negative feedback in order to maintain the target system within homeostatic parameters. These cycles can range in duration from minutes to months.





The major glands that constitute the human endocrine system are the hypothalamus, pituitary, thyroid, parathyroids, adrenals, pineal body, pancreas, and the reproductive glands. The brain, heart, lungs, kidneys, liver, thymus, skin, and placenta also produce and release hormones in order to regulate specific homeostatic processes with which they are associated. In most cases hormonal regulation addresses vital processes that are essential to survival. The receptors and activation patterns of target cells and organs associated with such processes required long periods of evolutionary time to adapt their function to the needs of the systems under regulation. The hormonal communication system does not learn quickly.



[2] Notwithstanding the fact that important links in the neural communication mechanism are dependent upon graded potential impulse conductance.

Important advantages of the neural communication system include speed, adaptability and learning, the ability to make fine discriminations about the environment and creative responses to it, the ability to store and manipulate symbolic information, and the ability to associate sensory and motor signals with their anatomical sources and targets. Important advantages of the hormonal communication system are its ability to integrate disparate and distributed nuclei, organs and faculties into coordinated functional subsystems, the ability to establish and sustain general patters of behavior by setting a neurochemical or emotional "tone" that recruits other subsystems to its purposes (including neural and cognitive subsystems), and the utilization of adaptive response patterns that have evolved over long periods of phylogenetic history.

Homeostasis↔Emotion↔Cognition

Distinctions between the neural and hormonal communication systems reflect their phylogenetic histories as clearly as do their common foundation in neurotransmitter mechanics. Their common origin is reflected in the fact that the general mechanics of hormonal transmission are nearly identical to those of neural transmission, except that a hormonal signal is delivered to its distant target by systemic fluid transport rather than by direct physical contact across a tiny synaptic cleft. In both cases the target cell must be equipped with chemical receptors that match the messenger molecule, and with intracellular elements that can express the chemical message as intended and then restore the local environment to readiness for the next signal or action. Illustrations of active mechanisms in hormonal and neural communication are remarkably similar, except for the fine details of neurotransmitter, protein, and enzyme messengers, the secondary chemical processes that they trigger, and the selective molecular channels and pumps that implement the electrochemical logic and clean up the environment.

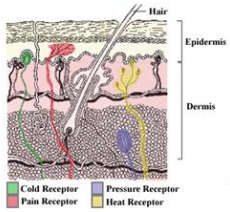
This continuity of signal mechanisms across the two systems highlights a basic tendency in evolution; to keep what works and improve it. This line of reasoning suggests that emotion is an extension and refinement of basic homeostatic mechanisms and that cognition is an extension and refinement of emotion (Watt, 2004). The overlap in the systems that support increasingly sophisticated hormonal and neural functions supports this interpretation and it makes sense of the continuity that is apparent in the spectrum of cognitive to emotional appraisal and response.

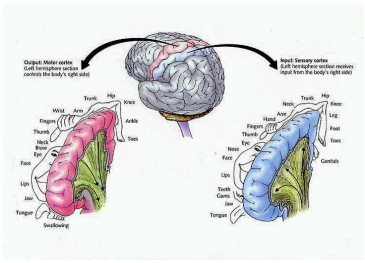
4) What is the function of the sensory system? How do the sensory receptors work? Describe the sensory pathways, including cortical fields and inputs, primary receptor circuits, and specialized receptors. What is the relation of "attention" to the sensory system? What part of the brain is thought to govern it?

The human sensory system integrates, transforms, and propagates information gathered from specialized external and internal receptors, through a hierarchy of cognitive systems that culminates in conscious perception and apperception. Interpretation of internal and external circumstances and responses to them are evoked, refined, and inhibited at multiple levels in the hierarchical sensory stream, ranging from reflex to deliberate executive action. Proprioception is routinely cited as a sensory modality along with the standard five, and it seems to me that at least one other interoceptive sensory modality should be specified in order to account for the conscious "perception" of memory and cognitive events, including dreams and imagination (Ferguson, 2004), although I have not found this intuition reflected in the literature that I have surveyed.

Sensory receptors and receptive fields

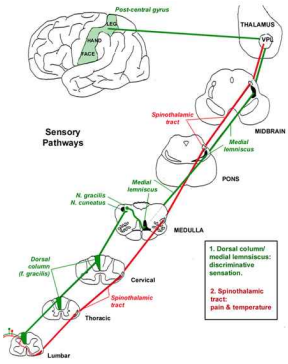
Each sensory receptor performs some particular transduction of energy into a digital signal that is propagated along the sensory stream by one or more action potential impulses. Sensitivity to various types of stimulation is achieved by a wide variety of neurons (called *neurones*) which react in various ways to detect movement, position, vibration, temperature, chemistry, electrostatic potential, or radiation. Like any other neuron, when the applicable threshold stimulation is reached at the axon hillock the neurone fires and transmits an action potential impulse upstream. The interpretation of such impulses is made within the context of each sensory channel. The range of environmental stimulus which is accessible to any particular element of the sensory stream is called that element's *receptive field*. At the level of individual neurones this designation is quite literal (e.g. the visual receptive field that is accessible to a particular retinal photoreceptor). The visual system as a whole can also be staid to have a visual field, which refers to a range of environmental conditions that is much more inclusive and far less literal. In many cases, the receptive field maps sense objects to some physical brain morphology, as in the homunculi of the motor and somatosensory cortices.



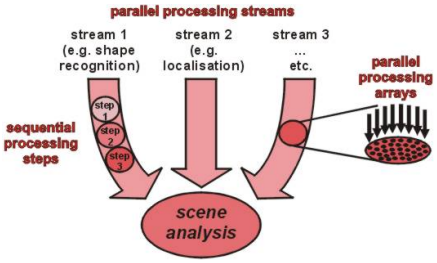


Sensory Pathways and Cortical Fields

Two major somatosensory pathways extend from the spinal cord to the brain: one for touch and proprioception (the posterior column) and the other for pain and temperature sensation (the spinothalamic pathway) which terminate in the thalamus. Complex modular visual, auditory, olfactory, and proprioceptive sensory channels also terminate in various formations within the thalamus, which distribute sensory and interpretive information to specialized primary and association cortices for further interpretation and encoding as perceptual qualia. The modular and massively parallel architecture of the sensory stream is naturally supported by the digital nature of the action potential signal, which is unattenuated by duplication at any number of axonal branches.

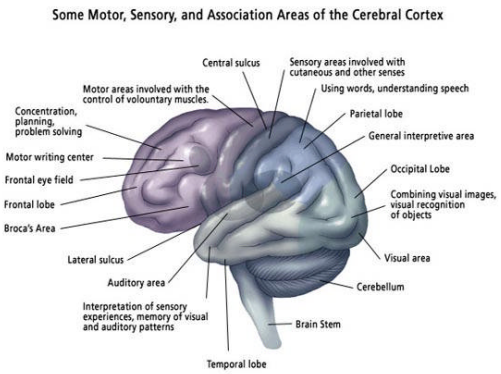


Each sensory stream is split several times in this way as different properties of the signal are evaluated in parallel, as illustrated by the schematic diagram for secondary visual processing. Sensory signals are consolidated, interpreted, translated, and summarized at each level of integration within the sensory hierarchy. At each level in the hierarchy there is the opportunity for increasingly global response; ranging from reflex action to deliberate strategy (Kolb & Whishaw, 2003).



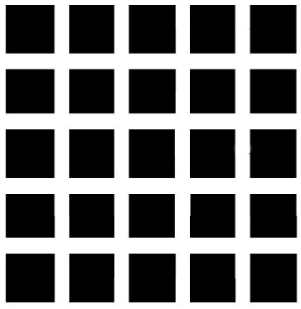
Somatosensory and Motor Cortical Fields

All mammals have at least one cortical area that is oriented toward each sensory system, and most have multiple secondary areas that are subordinated in various ways to each one. Each of the cortical areas consists of multiple modules that evaluate the sensory stream in parallel according to various criteria. For example, in their projections to the visual cortex, the systems for pattern perception, color vision, depth perception, and visual tracking are as anatomically independent from one another as are the systems that encode hearing and taste. Although the other sensory modalities do not command as much cerebral anatomy as vision, each sensory mode integrates multiple receptor types, parallel encoding, and often separate propagation paths up the sensory/cognitive hierarchy.



Attentional Discrimination and Neural Synchrony

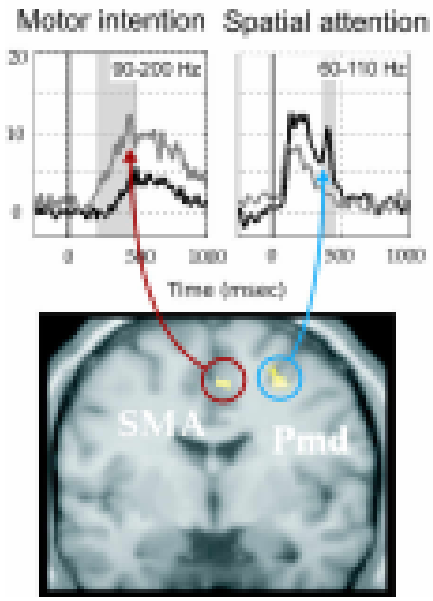
Attentional processes are pervasive throughout the sensory hierarchy, both because attention is the essence of discrimination and also because it conserves scarce computational capacity (Fidelman *et al.*, 1995; Yantis & Johnson, 1990). At the very head of the visual stream, in the retina, the mechanism of lateral inhibition imposes an arbitrary attentional criterion (sequence of signal detection) to reduce the number of bits that need to be transmitted along the optic nerve (Walley & Weiden, 1973). Nuclei further up the visual stream discriminate among the signals that they receive on the basis of criteria that progress from elementary orientation, contrast, and motion detection, through increasingly abstract levels of object identification and willful conscious attention. The pinnacle of the attentional tree appears to be effortful concentration on an object that is selected on the basis of purely abstract cognitive criteria, such as the instructions of either a researcher or a *guru*, which could be literally anything.



I recognize that this broad conceptualization of attention extends far beyond the usual emphasis on the contents of consciousness, but it is illuminating to regard conscious attention as the endpoint on a continuum of discrimination and resource allocation mechanisms at *every* level of organization. The further up the hierarchy, the more essential resource husbandry becomes, due to the increasing complexity of the subject matter and the range of possible alternatives. Think of the implications of "attention" to an receptive field as broad and abstract as intimate partner violence,

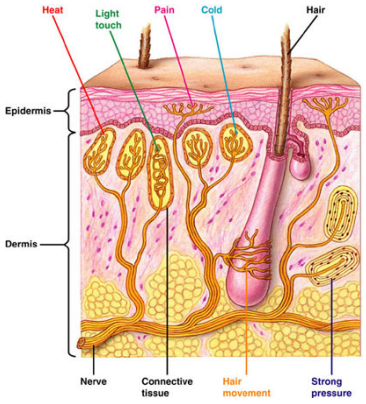
sustained at some significant level over a period of decades. This implies the selective activation and ongoing development of some very specific cognitive networks and behaviors, and the suppression of many others, as attention always does. Not only careers are defined in terms of attentional focus, but behavior and experience at every scale.

The mechanism of the attentional spotlight at higher levels of organization appears to be the temporal synchronization of firing patterns across whatever brain regions happen to be the focus of attention at any particular moment (Kaye & Ruskin, 1990; Koch & Crick, 1991; Yantis & Serences, 2003). Signal spike patterns in the gamma band (35 – 90 Hz) are associated with attentional tasks related to numerous cortical fields that are known to be related in relevant ways to the target stimulus. In fact, neural synchronization appears to serve a variety of essential functions throughout the nervous system, and EEG measures of synchronous neural spikes in the gamma range are broadly associated with attention and with consciousness itself (the 40 Hz signal that is always present in conscious subjects disappears under anesthesia). Although this mechanism is not well understood, fMRI and PET studies demonstrate activation of various frontal lobe sites, especially the anterior cingulate cortex, in association with attentional tasks (Kincade *et al.*, 2005). Extensive axonal projections from these areas to most other brain regions provide the top-down attentional mechanism that constitutes what we experience as voluntary and effortful attention.



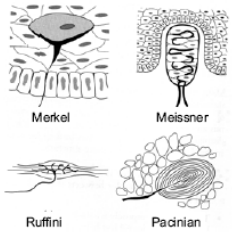
5) How are tactile sensations determined by skin receptors and joint receptors? How are pain signals transmitted? How do we localize specific tactile stimulation on a certain body part?

Somatosensory neurons that link cutaneous receptors to the central nervous system typically develop in clusters known as *ganglion* that are located near the spinal cord, from which they project afferent nerve fiber to bones, muscles, joints, and skin. These afferent projections are terminated in three main classes of receptor in the skin and the joints: mechanoreceptors, thermal receptors, and nociceptors. Distinct sensations of pain, warmth, cold, pressure, and vibration are produced by activity in these classes of sensory receptors and their associated afferent nerve fiber. Tactile receptors can be further subdivided on the basis of their response to continuous stimulation. Slowly adapting receptors generate signals for the duration of a constant stimulus, whereas rapidly adapting receptors gradually reduce their discharges in the presence of a steady stimulus until they reach a baseline level or cease firing entirely. More than one receptor class may contribute to a given sensation, and, in fact, sensations may differ depending on the relative contribution of different receptor classes.



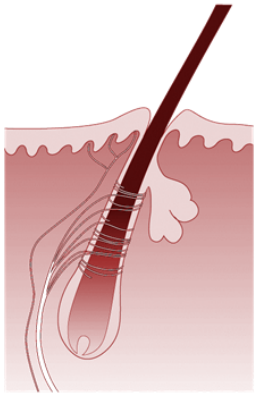
Receptors that Respond to Pressure: Mechanicoreceptors

A mechanoreceptor is a sensory receptor that responds to mechanical pressure or distortion. There are four main types of mechanoreceptors in humans: Pacinian corpuscles, Meissner's corpuscles, Merkel's disks, and Ruffini corpuscles. In hairy skin, Merkel cells enclose mechanical receptors within visible surface structures known as *touch domes*, and in glabrous (hairless) skin, Merkel disks are found at the base of skin ridges such as those that constitute fingerprints. Merkel disks also provide positional and tensional feedback from joints and certain flexible cartilage formations. These receptors transduce mechanical energy into nerve impulses that rise in frequency in proportion to the intensity of the stimulus, thereby informing the brain of the duration and magnitude of pressure or tension. Depending upon the morphological context in which these signals are interpreted (where they are coming from), they can be interpreted as indications of pressure, vibration, tension, or stretching.



Cutaneous Receptors Attached To Hairs

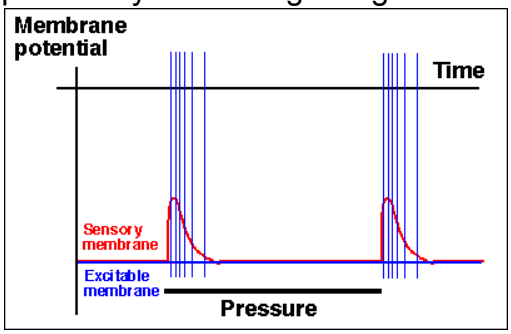
In hairy skin, specialized receptors that attach themselves to the base of the hair follicle are exceptionally sensitive to tactile stimulation. A typical hair is enveloped by a network of nerve terminals branching from five to nine large axons. In primates, these terminals fall into three categories: lanceolate endings, spindle-like terminals, and papillary endings. All three are rapidly adapting, such that a steady deflection of the hair causes nerve impulses only while movement occurs. Thus, these receptors are exquisitely sensitive to moving or vibratory stimuli, but provide little or no information about pressure, or constant touch.

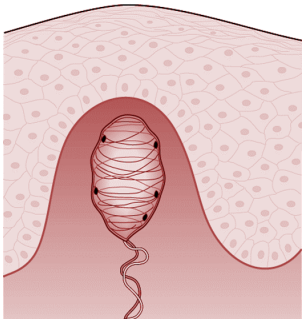


Lanceolate endings arise from a heavily myelinated fiber that forms a network around the hair and entangles itself among the cells at the base of the hair. Spindle-like terminals ascend to the sloping hair shaft and end in a semicircular cluster just below a sebaceous gland. Papillary endings are similar to spindle-like terminals except that, instead of ending on the hair shaft, they terminate as free nerve endings around the orifice of the hair.

Cutaneous Receptors in Glabrous Skin

The Pacinian corpuscle is a rapidly adapting receptor that, when subjected to sustained pressure, produces an action potential impulse only at the beginning and the end of the stimulus. It responds to relatively high-frequency vibrations, in the range from 80 to 400 Hz, and is most sensitive around 250 Hz. These receptors respond especially well to vibrations transmitted along bones and tendons. In addition to the Pacinian corpuscle, there is another rapidly adapting receptor in glabrous skin known as Meissner's corpuscle, which is responsive to low-frequency vibrations in the range from 2 to 40 Hz. This receptor consists of the terminal branches of a medium-sized myelinated nerve fiber enveloped in one or several layers of what appear to be modified Schwann cells, called laminar cells, which connect to basal cells in the epidermis. If Meissner's corpuscle is selectively inactivated by local anesthetic, the sense of flutter or low-frequency vibration is lost. This suggests that it functionally complements the high frequency capacity of the Pacinian corpuscles. Together, these two receptors provide neural signals sufficient to account for human tactile sensibility to a full range of vibrations.





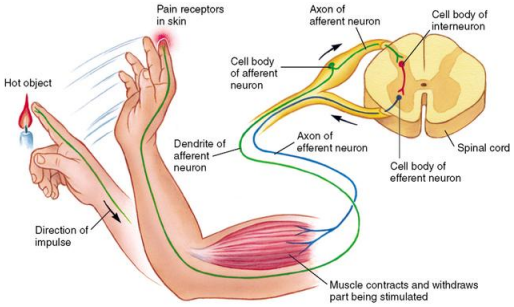
Mysterious Receptors that Respond to Temperature: Thermal Receptors

Normal temperature sensitivity is relative, and there is clearly some distinction among the free nerve endings in the receptors that respond separately to changes in coolness and warmth. The mechanism(s) of sensitivity to heating and cooling are not well understood, and even the conclusion that they are served by separate receptors derives from the empirical observation that warmth and coolness are detectable at different depths in the skin.

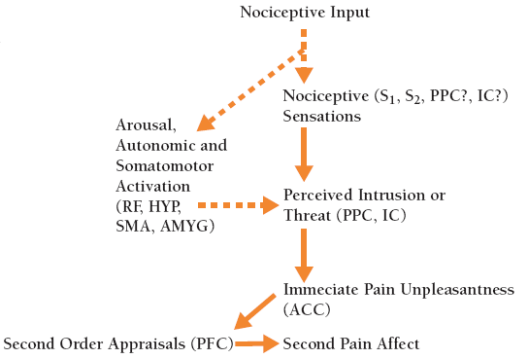
Receptors that Respond to Pain: Nociceptors

There are several types of nociceptors, classified according to the stimulus modalities to which they respond: thermal, mechanical or chemical. These receptors allow the organism to feel pain in response to damaging pressure, excessive heat, excessive cold and a range of chemicals, the majority of which are damaging to the surrounding tissue.

As pain signals are propagated along the somatosensory pathway to the central nervous system, they may trigger a classic reflex arc known as nociceptive withdrawal reflex (NWR) intended to protect the body from damaging stimuli. The classic example is the reflex withdrawal from a hot object. The heat stimulates temperature and pain receptors in the skin, triggering a sensory impulse that travels to the central nervous system. The sensory neuron also synapses with interneurons that connect to motor neurons. Some of these send motor impulses to the flexors to allow withdrawal; some motor neurons send inhibitory impulses to the extensors so flexion is not inhibited, which is known as reciprocal innervation. While this occurs, other interneurons relay the sensory information up to the brain so that the situation can be evaluated at a more global level and an appropriate action can be taken.

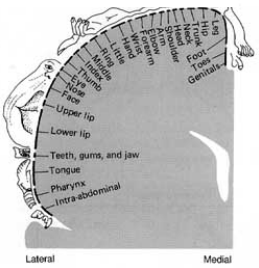


Cortical activation resulting from painful stimulus is much more global than most that which is associate with most other types of sensory stimulation, which tend to be mediated much more tightly by the related primary and secondary cortical fields. This is presumably due to the potentially critical threat to survival that pain represents, and interactions are rapidly initiated along the ascending somatosensory pathway to stimulate a network of brain structures that process nociceptive information in parallel. Spinal pathways to the amygdala, hypothalamus, reticular formation, medial thalamic nuclei, and various limbic cortical structures provide direct stimulation to the formations most closely involved in arousal, homeostatic regulation, and affect. Prefrontal and executive functions are stimulated later and may serve to inhibit the more immediate reactions that results from nociceptor stimulation.



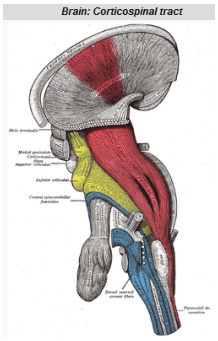
Localization of Tactile Stimulation

The localization of tactile sensation is inherent in the connectivity of sensory streams from various parts of the body onto the primary sensory cortex, which can be interpreted as a map of somatosensory space. This funny looking guy is called a homunculus, whose parts are drawn in proportion to their representation on the primary sensory (or motor) cortex. There is debate about how this somatic mapping works, how literally to take the topological metaphor, and how many homunculi are actually mapped on the motor and sensory strips. Localization is certainly not *entirely* dependent upon physical connectivity, however, as neural plasticity illustrates. Often, when injury is sustained to the sensory or motor cortices, higher priority requirements displace cortical services elsewhere in homuncular space. Somatosensory localization can therefore also be learned.



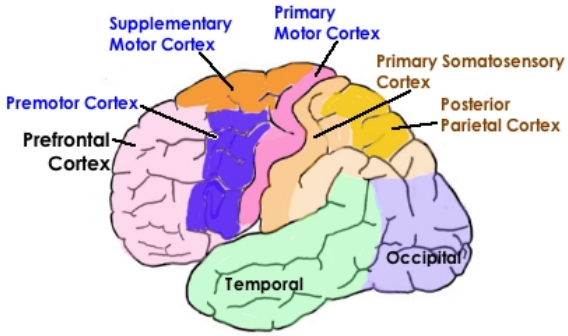
6) Describe the structures and known functions of the pyramidal and extrapyramidal systems.

The pyramidal motor system is primarily responsible for initiating all voluntary movements in the modern primate nervous system. It constitutes the main channel of motor signals from the primary motor cortex to the spinal column (red highlight in the illustration at the right) and thence to the various moving parts of the body. The extrapyramidal motor system is phylogenetically older than the pyramidal system, which it now both modulates and subserves. The extrapyramidal motor system is more exclusively responsible for motor behavior in lower vertebrates.

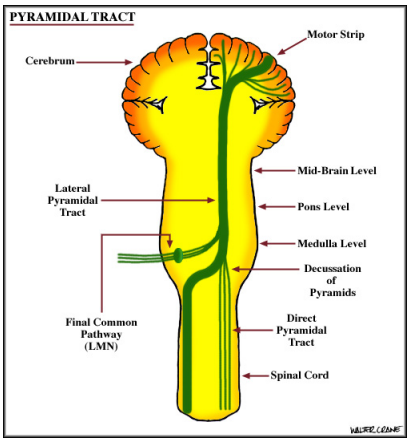


The Pyramidal Motor System

The Pyramidal motor system is co-called because either a) the large cell bodies and the humongous long axons descending from layer 5 of the primary motor cortex resemble pyramids (Carlson, 2001), or else because b) the bumps on the ventral brainstem at which the corticospinal tracts terminate resemble pyramids (Kolb & Whishaw, 2003). In any event, the pyramidal system represents what might be thought of as the official chain of command in the neocortical motor system. The prefrontal cortex sits at the head of the primate executive motor stream conducting global environmental assessment, concocting strategic and tactical plans, and initiating voluntary undertakings of arbitrary complexity.



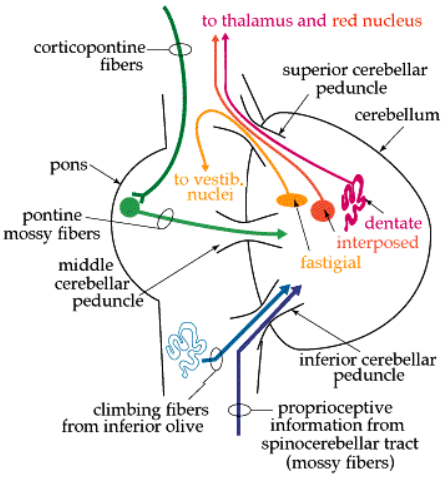
To continue the military metaphor, the prefrontal cortex issues action orders to the premotor cortex, where they are operationalized as a sequence of motor operations that is composed from a repertoire of behavioral skills. These sequenced instructions are communicated to the primary motor cortex, where they are modulated by input and feedback from the sensory cortices and from the secondary motor cortex. There is also extensive horizontal synaptic connectivity among various regions of the primary cortex itself. Relatively primitive motor instructions are propagated from appropriate homuncular segments of the primary motor cortex, along two axonal bundles called the *corticobulbar* and *corticospinal* tracts, which descend to the brainstem. The corticobulbar tract terminates there in nuclei which control facial and other cranial musculature, and the corticospinal tract terminates in the vicinity of the motor neurons on either side of the spinal cord that control movement in the limbs and body.



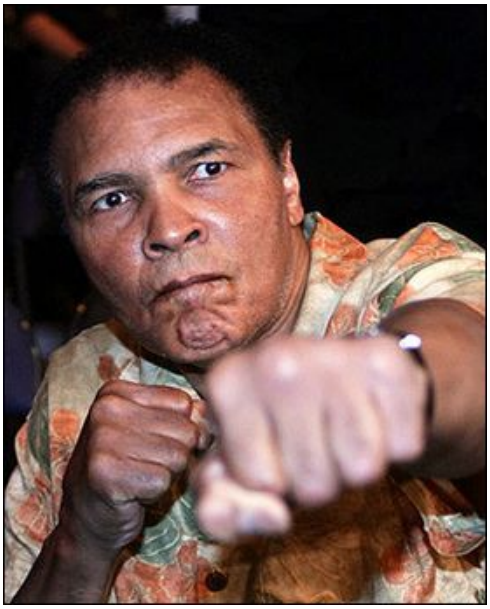
All of the structures upstream from the primary motor cortex (the prefrontal, premotor, secondary motor, and sensory cortices) also maintain direct axonal projections to lower levels in the motor hierarchy, down to the level of individual motor ganglia, and indirect projections through the various structures of the extrapyramidal system. Beating the military metaphor nearly to death, the brass continues to meddle in the details of execution, at their whim, up and down the chain of motor command.

The Extrapyramidal Motor System

The extrapyramidal system dampens erratic motions, maintains muscle tone and enhances stability and fine motor coordination. It is phylogenetically older that the pyramidal system and plays a relatively more important role in non-primates. Many of its synaptic connections are extremely complex and poorly understood. The extrapyramidal nuclei include the substantia nigra, caudate, putamen, globus pallidus, thalamus, red nucleus and the subthalmic nucleus. All of these nuclei are synaptically connected to one another, to the brainstem, the cerebellum and to the pyramidal motor system. The extrapyramidal system therefore supports, modulates, and refines the execution of motor expression that may be initiated at every level from deliberate and explicitly planned movement through the extended execution of automatic learned behavior sequences like walking, typing, driving, and routine weapon maintenance or carpentry.

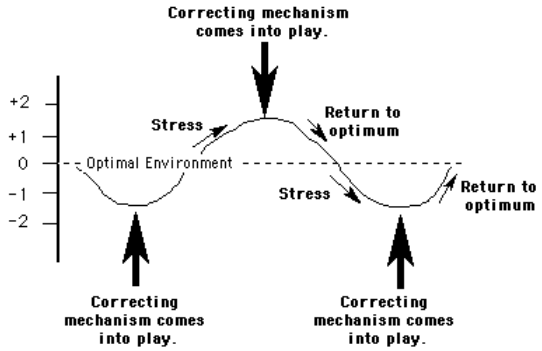


Although the efferent mechanism of the extrapyramidal motor system is not well understood, disturbances in the structures listed above have pervasive effects on both voluntary and involuntary motor expression. There are two major classifications of movement disorders that result from dysfunction of extrapyramidal motor structures, *dystonias* and *dyskinesias*. Dystonias are spasms of individual muscles or groups of muscles. They can be sustained or intermittent, sudden or slow, painful or painless, and they can affect any of the voluntary muscles including those of the vocal cords. Dyskinesias are involuntary, often hyperkinetic, random or rhythmic movements that have no apparent purpose. Dyskinesias can affect the ability to initiate or stop a movement as in Parkinson's or they can affect the smooth movement of a joint resulting in a jerky articulation. Abrupt and seemingly violent movements of a limb are common as are gyrations of any body part. Tics and involuntary vocalizations are related to dyskinesias.



7) Temperature regulation and fluid volume control are important survival skills for all organisms. How are these functions controlled in humans?

The process of maintaing biochemical factors within a particular range is known as homeostasis, and in most cases a wide variety of mechanisms exist at different levels of organization in order to maintain it, ranging from local cellular chemistry to broad behavioral strategies that involve the whole organism over considerable periods of time. The emphasis here will be on the neurological aspects of homeostasis for the maintainence of fluid volume and internal body temperature, in which the hypothalamus plays a central role.

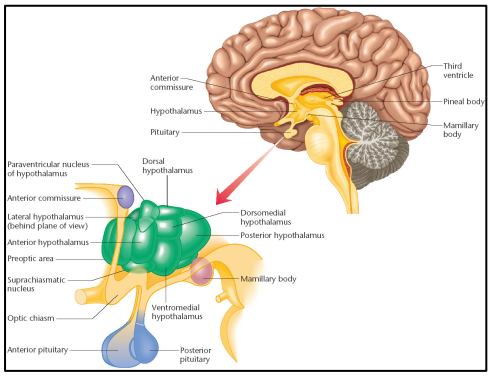


Any homeostatic regulatory mechanism must incorporate four fundamental elements: 1) the environmental variable to be managed, 2) a set point at or near which that variable is to be maintained, 3) a mechanism to evaluate the target variable, and 4) a correctional mechanism that can be triggered to draw the variable back toward the set point when it drifts outside the target range. Most homeostatic processes operate on the basis of negative feedback in the sense that they work to reverse trends that drift out of tolerance.

The Role of the Hypothalamus in Homeostasis

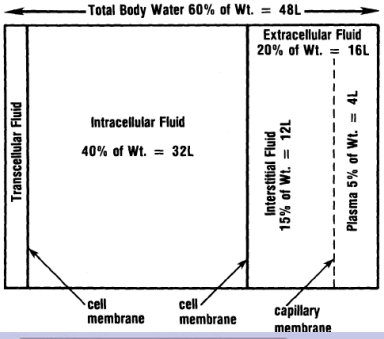
Homeostatis is an important function of the hypothalamus, which acts to maintain several biochemical factors, including fluid volume and intenal temperature, within a narrow range. In addition to thermoreceptors and osmoreceptors in the body of the hypothamamus, which monitor temperatire and fluid ionization directly, the hypothalamus also receives and integrates inputs from other formations about the state of the body and its environment, including:

- Nucleus of the solitary tract: visceral information including blood pressure.
- Reticular formation: tactile information including skin temperature.
- Organum vasculosum laminae terminalis (OLVT): located along the ventricles outside the blood-brain barrier, sensivity to changes in the electrostatic potential (ionic balance) of the extracellular fluid.
- Limbic and olfactory systems: the amygdala, the hippocampus, and the olfactory cortex all project extensively to the hypothalamus.

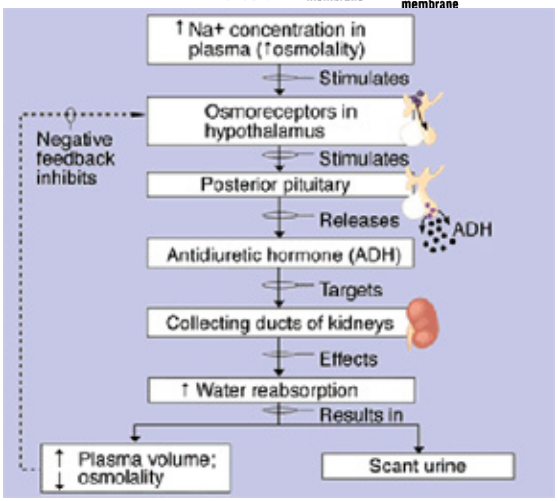


The hypothalamus intiates corrective action of various kinds either by means of neural signals to the medulla, which regulates the autonomic system, or else by means of endocrine signals to the pituitary, which indirectly influences every endocrine gland in the body.

Regulation of Fluid Volume

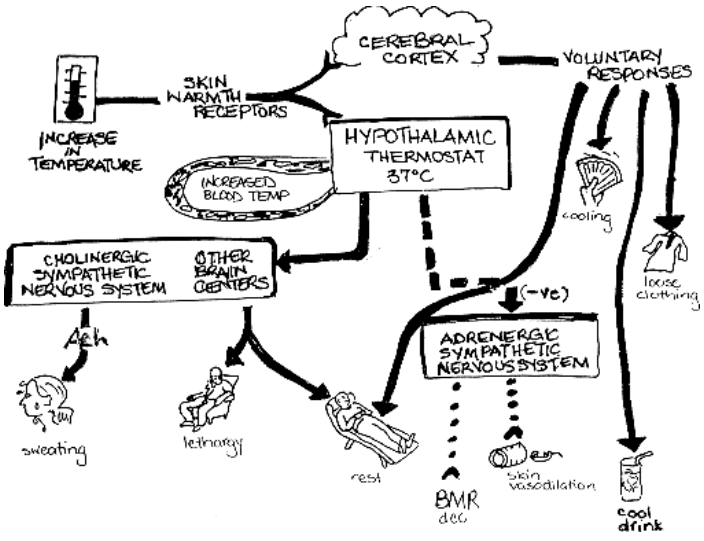


The hypothalamus regulates the volume of extracellular fluid in the body most immediately by monitoring its salinity and either inhibiting the kidneys from expelling water or leaving it free to do so. When fluid volume decreases, sodium concentration in the blood increases. The increased sodium eventually stimulates osmoreceptors in the hypothalamus, which causes the posterior pituitary gland to release an antidiuretic hormone (ADH), which inhibits the kidneys from excreting water in the urine. The extra water returns the blood volume to normal and thereby maintains homeostasis for fluid balance. Intracellular fluid balance is regulated indirectly by this mechamism, since the intracellular fluid maintains an equilibrium with the extracellular medium by osmosis. Longer term regulation of fluid balance in the system is accomplished by stimulating the cerebrum, which eventually generates feelings of thirst and the fluid seeking behavior that is attendant it.



Regulation of Body Temperature

When the internal or external temperature falls, signals are sent from the thermoreceptors in the skin and deep tissue, or via the bloodstream, to the cerebral cortex and to the hypothalamus. The cerebrum makes the person aware of being cold, which can result in voluntary sweater-seeking behavior, while the hypothalamus stimulates the anterior lobe of the pituitary gland to release a hormone into the bloodstream, which stimulates the thyroid to produce norepinephrine, epinephrine, and thyroxin which, in turn, stimulate cellular metabolism to generate heat. The hypothalamus also stimulates the sympathetic system by neural signals to the medulla, which increases the activity of muscular and other systems, restricts blood flow near the skin surface, reduces sweating, and eventually induces shivering.



When it is too warm all of these heat-generating activities are suspended and, as a result of other positive actions that utilize the same efferent pathways as the heating corrections, blood is diverted to areas near the skin and sweating is stimulated, which is an extremely efficient means of shedding excess thermal energy by evaporation.

8) Describe the typical human sleep-wake cycle. What are the characteristics of each part of the cycle, and how do these characteristics change over the lifespan? What brain structures and neurotransmitters are thought to be involved?

Sleep Assessment and the Sleep Cycle

The systematic characterization of sleep stages generally relies on the following three physiological measures:

1. Gross brain wave activity as measured by an electroencephalogram (EEG).
2. Muscle tone as measured by an electromyogram (EMG).
3. Eye movement as recorded by an electro-oculogram (EOG).

Each sleep stage exhibits a distinctive EEG, while the EMG and EOG also characterize rapid eye movement (REM) sleep. REM sleep is characterized by desynchronization of the EEG, loss of muscle tone, and sympathetic nervous system activation; whereas non-rapid eye movement sleep is characterized by parasympathetic nervous system activity. REM sleep accounts for about 25% of total sleep time. The typical human sleep cycle consists of 4 or 5 stages of sleep, depending upon whether or not the initial transition from waking to sleeping (somnolence) is counted as part of the cycle, as I will count it here. The following 4 stages normally repeat themselves in sequence, over the course of about 90 minutes, from 5 to 7 times a night.

Stages of Sleep

Stage 1 (somnolence): The alpha rhythms (8-12 Hz) that characterize all waking states diminish dramatically and theta rhythms (4-8 Hz) appear in the EEG. Phenomenologically, this is the state of drowsiness and it serves as a transitional state of consciousness between waking and sleep. During stage 1 there is some lose of muscle tone and the limbs are subject to sudden twitches. Awareness of external stimulus diminishes and, if the transition to stage 2 sleep is completed, no memories of environmental stimulus during this period are reported later. If subjects are aroused at this point, however, they generally deny having been asleep and can report environmental stimulus to which they were exposed prior to arousal. Stage 1 sleep normally lasts 10 or 15 minutes.

Stage 2: Muscle tone and heart rate both decline and responsiveness to the environment disappears completely. At this stage the EEG exhibits apparently random periodic bursts of activity, in the range of 12-16 Hz, known as "sleep spindles" and also of very brief high voltage peaks, called "K-complexes." These odd electrostatic artifacts may serve specifically to disturb ongoing large scale patterns of neural synchronization across the brain in preparation for the next sleep state; clearing the decks for new thoughts and dreams, if you will (Crowley *et al.*, 2004). Like a meditation docent's chimes or gong. Stage 2 occupies about half of normal sleep time.

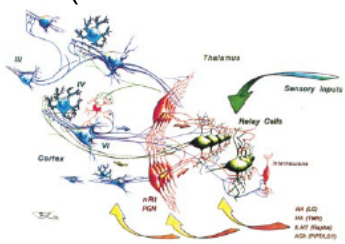
Stage 3 (slow wave sleep): Spindles and K-complexes disappear from the EEG at the onset of stage 3 sleep and low frequency rhythms (.5–4 Hz) predominate. This stage is therefore referred to as slow wave sleep (SWS) and it apparently serves primarily as a transition to deep sleep. SWS occupies about 5% of normal sleep time.

Stage 4 (deep sleep): This is the deepest stage of sleep, dominated by even delta rhythms, and it is difficult to wake a subject in this state. When aroused from stage 4 sleep subjects are disoriented and may be unable to produce a phenomenological report of their recent experience. Deep sleep predominates during the first third of the night and accounts for about 15% of normal sleep time overall.

Stage 5 (REM sleep): This is the stage of sleep in which EEG activity most closely resembles waking patterns, with erratic breathing and heart rate as well as heightened synchronous activity in all brain regions. REM sleep is stimulated by a formation in the brainstem known as the *pontine tegmentum*, which also shuts down the production of several neurotransmitters and inhibits motor signals to induce *REM atonia*, or muscular paralysis. This is presumably so that we don't act out our dreams in the real world while we are asleep.

Regulation of sleep

The sleep cycle is regulated primarily by formations in the brain stem and thalamus, and by various hormones produced in the hypothalamus (Salin-Pascual *et al.*, 2001). Adenosine accumulates in the brain during wakefulness and decreases during sleep, and norepinephrine, serotonin and histamine production are all suppressed entirely during REM sleep. The *suprachiasmatic nucleus* of the hypothalamus receives projections directly from the optic nerve and plays an important role in maintaining circadian and other rhythms. In the presence of light it sends messages to the pineal gland that suppress its production of melatonin.



Finally, as with most homeostatic systems in the body, the higher faculties of the cerebrum are recruited to provide logistical support and environmental conditions conducive to sleeping at regular intervals. Such voluntary behavior is motivated by the sensation of sleepiness, or a fear of it. Endocrine, neurological, and environmental factors therefore combine to regulate sleep and the sleep cycle according to both homeostatic and rhythmic criteria.

Changes in the Sleep Cycle over the Lifespan

Total sleep time for normal human beings peaks at birth and generally declines thereafter over the lifespan, although total sleep time typically becomes shorter during childhood and then lengthens again in adolescence. The percentage of REM sleep is highest during infancy and early childhood, drops off during adolescence and young adulthood, and decreases further in older age, although the REM occurs earlier and each episode continues longer. Stages 3 and 4 in the first sleep cycle shorten dramatically in older people, so older people get less total deep sleep.

SLEEP NEEDS OVER THE LIFE CYCLE

Infants/Babies*	0-2 months: 10.5-18.5 hours 2-12 months: 14-15 hours
Toddlers/Children*	12-18 months: 13-15 hours 18 months - 3 years: 12-14 hours 3-5 years: 11-13 hours 5-12 years: 9-11 hours
Adolescents	8.5-9.5 hours
Adults/Older Persons	On average: 7-9 hours

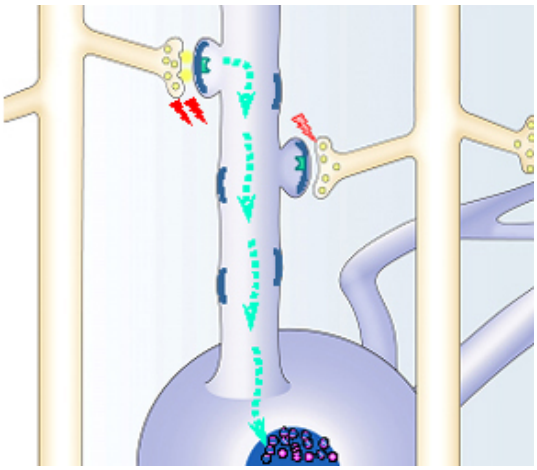
*Total time includes naps.

9) Learning and memory storage have been demonstrated to result in anatomical and chemical changes in the brain. What are the changes, and how were they found?

> *"When an axon of cell A is near enough to excite a cell B and repeatedly and persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficacy, as one of the cells firing B, is increased."*
>
> - Donald Hebb (Rosenzweig, 1996)

The Hebb Rule

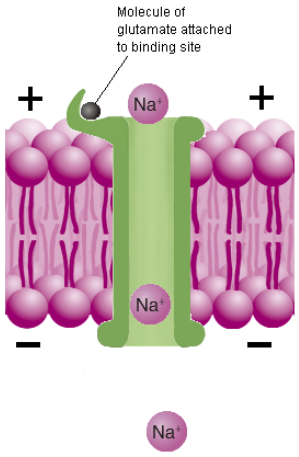
This formulation of the most fundamental mechanism of learning and memory (which are identical for present purposes) is known as the *Hebb rule* or the *Hebb postulate*, and it is reflected in the popular phrase "*neurons that fire together, wire together.*" While the functional significance of learning and memory must be understood at the level of neural networks within and across brain regions, they all rest on the mechanics of individual synaptic plasticity that are responsible for implementation of the Hebb rule on different timescales. At the time that Hebb made this famous conjecture, in 1949, he had no idea what the mechanism for this process might be, but it was already clear that the neural network architecture of the brain requires that the strength of individual synaptic connections be malleable in order for learning to take place. In fact, it turns out that the Hebb rule describes the neural mechanism of learning almost exactly, except that much of the relevant interaction actually takes place among the many dendritic spines of individual neurons rather than between nearby cells.



Physical and chemical reinforcement of a synapse in order to increase it's sensitivity to stimulation is called long term potentiation (LTP), and it is the basis of most learning and memory. Several different LTP mechanisms have been identified across almost every region of the vertebrate brain, but the most pervasive mechanism is associated with the specialized post-synaptic *NMBA receptor*, which I will describe below (Whitlock *et al.*, 2006). This form of long term potentiation relies upon an electrostatic spike that is generated along the dendritic spine of a certain class of neuron when the associated axon fires. The dendritic spike briefly sensitizes *all* of its spines to the NMBA receptor mechanism, which facilitates long term potentiation in any spines that are subsequently activated, even weakly, before electrostatic equilibrium is restored. This is the basic associative mechanism at the root of the NMBA mechanism and it implements the Hebb rule almost exactly. It is now clear that anatomical and chemical changes in the strength of synaptic connections occur systematically throughout the brain, and that memory is a highly distributed phenomenon. Long term potentiation is the neurochemical basis of memory and learning.

Common Glutamate (AMPA) Receptors

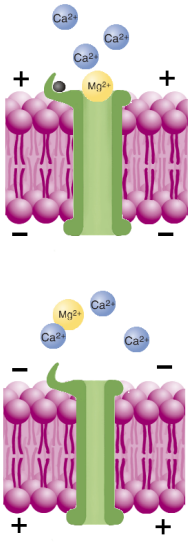
The most common type of post-synaptic receptor is the AMPA receptor, which serves as a sodium ion gate that is activated by the common neurotransmitter glutamate. When an action potential impulse arrives at the terminal button of an axon, glutamate is released into the synaptic cleft, which it traverses by diffusion to activate an AMPA receptor. The activated receptor opens a sodium channel that permits positively charged sodium ions from the interstitial fluid to migrate across the postsynaptic membrane, altering the internal polarization of the dendrite and contributing to whatever network logic that node happens to be participating in at the moment. The sodium ions are then returned to the interstitial fluid by means of the sodium pumps described in question #2, above, restoring the synapse to its original resting potential. This constitutes the normal work of the synapse in which a signal has been transmitted, but in which no learning has taken place. The next action potential that arrives at such a terminal button will have exactly the same effect as the first.



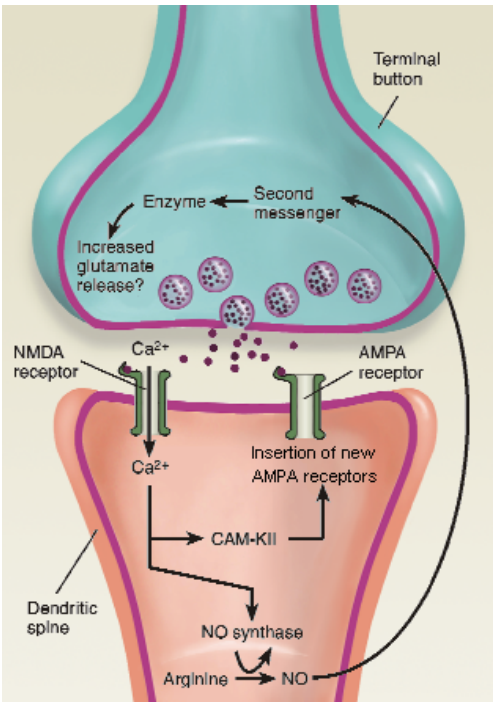
The NMBA Receptor Mechanism of Long Term Potentiation

The first actual observation of long term potentiation (LTP) was made in 1966 by Terje Lømo who conducted a series of experiments on rabbits to explore the role of the hippocampus in short-term memory. After isolating the connections between two regions of the hippocampus, Lømo observed that changes to the electrostatic potential in the one of these regions could be elicited by stimulation of the other, as he expected. However, Lømo also accidentally found that the postsynaptic responses to these single-pulse stimuli could be enhanced by delivering a preliminary electrical impulse immediately beforehand. When the synapse was primed in this way, he found that subsequent single-pulse stimuli elicited stronger effects, and that this enhanced sensitivity continued for several hours. A variety of neurochemical processes have since been found to account for this effect, most of which operate in a manner similar to the following NMBA receptor mechanism.

NMBA receptors are essentially calcium ion gates that open in response to glutamate stimulation only when the post-synaptic membrane is depolarized from its normal state, which happens for a short period immediately after the host neuron has fired. Under conditions of normal polarization a magnesium ion blocks the calcium channel (top right), but when the polarization of the membrane is briefly reversed by the electrostatic backwash of an action potential firing the magnesium molecule is displaced (bottom right). If a glutamate messenger arrives during this brief period, it opens the NMBA channel and allows calcium ions to migrate across the membrane. NMBA activation therefore requires *both* depolarization by the electrostatic backwash from the host neuron firing *and* concurrent glutamate stimulation, even weak stimulation, by the terminal button of another neuron, precisely as specified in the Hebb rule.



The migration of calcium ions across the post-synaptic membrane triggers a series of chemical reactions that produce structural changes on both sides the synapse that strengthen its potency. Although the precise chemistry of this process is not yet well understood, the calcium sequence activates proteins, which are ambient in the post-synaptic fluid, that duplicate existing AMPA receptors in the membrane. Duplication of AMPA receptors doubles the potency of the synapse in a linear way. The calcium sequence also results in the synthesis of small quantities of nitric oxide (NO), to which both the post-synaptic and the pre-synaptic membranes are permeable. The NO diffuses across the interstitial fluid to penetrate the membrane of the terminal button, where it acts as a retrograde messenger (carrying the signal back) that somehow results in an enhanced capacity to release glutamate in response to subsequent action potential impulses. NO is rapidly degraded in the interstitial fluid, so its action is limited to a very short diffusion radius around the dendritic spine, which confines the action mostly to the associated terminal button rather than to others in the neighborhood.

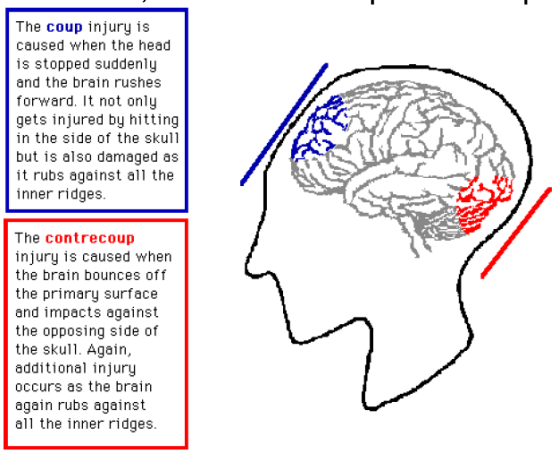


Long Term Depression

Long term potentiation provides the neurochemical mechanism that accounts for most learning and memory, and an incredible range of neural network relationships can be established in this way. But the capacity of even so vast a neural network as the human brain is limited and a maintenance function is necessary in order to return lightly utilized synapses to the “available” pool of neutral nodes. Most synapses that are capable of long term potentiation are also capable of long term depression, which effectively reverses the effects of long term potentiation. In the case of the NMBA receptor mechanism, the effects of LTP are reversed in a linear way by instances of weak synaptic stimulation that is *not* accompanied by a reversal of polarity in the backwash of an axonal firing. This is the neurochemical basis of learning and memory extinction.

10) Describe the probable effects of a left-hemisphere closed head injury. If the lesion is anterior, what type of impairment would be expected? If it is more posterior? Under what circumstances might we find an exception to the above?

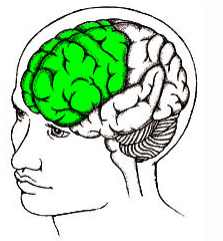
Closed head injuries tend to be diffuse, but lesions are typically more severe at what are known as the *coup* and *countercoup* locations, which are the point of impact and the opposite side of the skull, against which the brain may rebound. Closed-head injuries are generally accompanied by a loss of consciousness, which typically results from strain on fibres in the reticular formation of the brainstem. The severity of closed head injury is generally indicated by the amount of time spent unconscious, which correlates directly with subsequent mortality, intellectual impairment, and deficits in social skills (Lezak, 1979). Two kinds of impairments are observed following closed-head injuries:



1. **Discrete impairments** related to cortical lesions at the site of the coup or countercoup. These are most commonly associated with damage to the frontal or temporal lobe. Damage to the left hemisphere will tend to result in disturbances of speech or verbal comprehension (both Broca's area and Wernicke's area are in the left hemisphere), in the ability to master new tasks and manual skills (Kimura, 1977), and in motor difficulties on the right side of the body. If the primary lesions are anterior the ability to plan and organize is likely to be particularly impaired, emotional responses may tend to be inappropriate, and there is a much greater likelihood of major depression with any sort of anterior left-hemisphere damage (Aström *et al.*, 1993). If the primary lesions are more posterior it is likely to result in hearing impairments as well as increased irritability, impulsivity and frustration. Exceptions to these effects might be expected when previous neurological or developmental problems have resulted in shifting dependency for plastic functions to other brain areas, or when the subject is left-handed.
2. **Generalized impairments** resulting from diffuse cortical damage and generalized axonal shearing due to rotation of the brain within the skull or of the hemispheres with respect to one another. These are characterized by a loss of mental speed, concentration, and overall cognitive efficiency.

11) Compared to other animals, the frontal lobes of humans are quite large. What are the effects of injury to this region of the brain? What are the effects of injury to the parietal region?

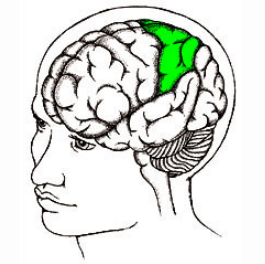
Injury to the Frontal Lobes



The frontal lobes are the most extensively connected region of the brain, and are widely considered to be responsible for much our personality. The frontal lobes are extremely vulnerable to injury due to their location near the surface at the front of the skull, and to their large size. The frontal area is the most common region of injury following mild to moderate traumatic brain injury (Levin & Kraus, 1994) and there is no other part of the brain where injuries can cause such a wide variety of symptoms (Clark *et al.*, 2004; Johnstone *et al.*, 1995). The frontal lobes are involved in motor function, problem solving, spontaneity, memory, language, initiation, judgment, impulse control, as well as in a wide range of social and sexual behavior. Effects of injury to the frontal lobes include:

- Loss of movement in various body parts, or paralysis.
- Changes in personality.
- Language problems.
- Difficulty with problem solving.
- Inability to plan a sequence of complex movements.
- Loss of spontaneity in social interaction.
- Loss of flexibility in thinking.
- Repetitive thoughts and obsessive behavior.
- Loss of attention or concentration.
- Emotional labiality.

Injury to the Parietal Lobes



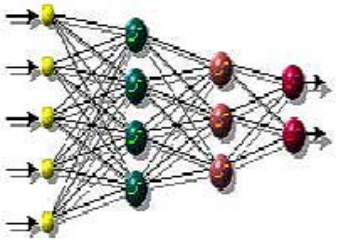
The parietal lobes are concerned with integrating sensory input with spatial referents generally, and primarily with regard to visual stimulus (Karnath, 1997). The parietal lobes include the primary sensory cortex, which is responsible for the integration of tactile sensations. Behind the primary sensory cortex is a large association area that controls fine sensation such as the evaluation of texture, weight, size, and shape. Damage to the parietal lobes often results in distortions of body image and spatial perceptions. Effects of injury to the parietal lobes include:

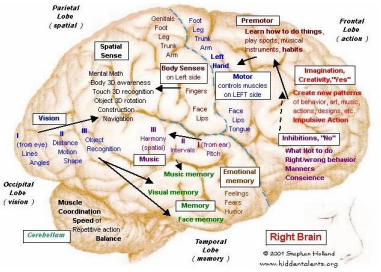
- Loss of hand-eye coordination.
- Difficulty in distinguishing left from right.
- Loss of awareness of body parts and/or surrounding space.
- Difficulty maintaining visual attention.
- Difficulty naming objects and with nouns generally.
- Distortion of the proportions in drawn objects.
- Inability to attend to more than one object at a time.
- Difficulty in reading and writing.

12) Neurospecificity of neural pathways and synapses according to an innate genetic map is widely accepted by some, contested by others. What is some of the evidence for and against neurospecificity, and what are some other determinants of nervous system development?

The Brain is Not a Sausage

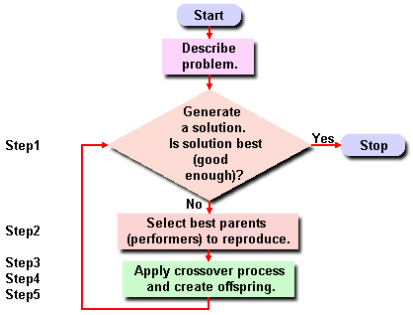
At the first *Toward a Science of Consciousness* conference that I attended in Tucson in 1996, the prominent neuroscientist Rodolfo Llinas delivered a keynote address entitled "The Brain is Not a Sausage" (Hameroff *et al.*, 1996). This title was intended as a counter-weight to what he saw as the infatuation of cognitive scientists with neural network models of psychological and cerebral functions. In fact, since neural networks are instantiations of the Universal Turing Machine, they can replicate the logic of *any* formal algorithm or natural system, including all psychological and mental faculties. Indeed, it is certainly the flexibility of neural networks in the brain that enables the higher human faculties of learning and memory to encompass arbitrarily diverse and abstract constructs, as they do. Recognition of the power of neural networks and the role that they play in the brain, in light of the many impressive instances of neural plasticity that have been established (see below) makes it tempting to over-generalize the plasticity of the human nervous system. Llinas' point was that while there may be many ways to implement any neural function *in principle*, the human brain has evolved highly specific neural mechanisms to support each of its vital functions, and that the brain cannot be properly understood without reference to the specialized functions of the various brain structures and their individual patterns of interconnectivity. The brain is not a sausage.



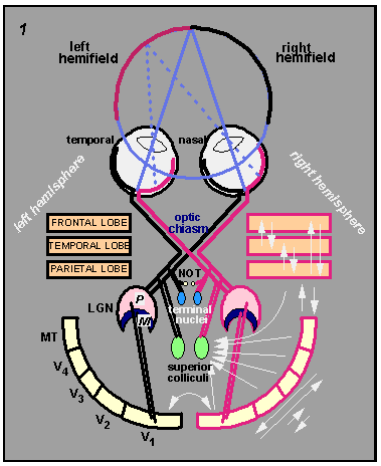


The Neurospecific Substrate of Neural Plasticity

Like nature *versus* nurture, the neurospecificity debate is a red herring. While it is true that any Universal Turing Machine can execute any algorithm 1) it must always be implemented in some specific hardware and, 2) enormous efficiencies can often be gained for a given function through the use of idiosyncratic algorithms that need not be based on any general theory or architecture. There is a vigorous field of computational theory that is based on the application of genetic algorithms to identify efficient solutions for a wide range of problems without the guidance of any theoretical model (Riveros *et al.*, 1995; Srinivas & Patnaik, 1994). This is exactly the means by which human brain functions actually evolved so it should be no surprise to find basic mental functions implemented in highly idiosyncratic (neurospecific) ways, as they clearly are. The more essential a function is to survival the more likely it is that such a mechanism will be found. Neural plasticity is a high-level capacity that sits at the very top of a complex hierarchy of highly neurospecific underlying mechanisms. Neural plasticity exists mostly at the level where we can change our mind about something.

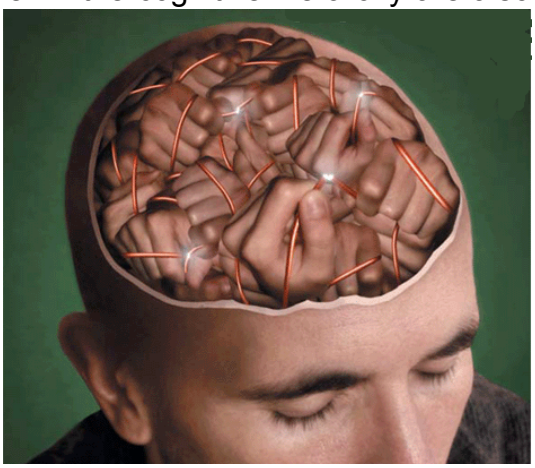


Take the highly specific architecture of the primate visual stream as an obvious example. Since the action potentials that transport information among the various structures of the visual system are essentially digital signals, their interpretation is entirely dependent upon the context in which they are received and reacted to. The only reason that a spike on the optic nerve can be interpreted as a particular retinal image at the lateral geniculate nucleus is that these structures have evolved in the context of their particular physical relationship. This is the case with the overwhelming majority of sensory systems and with most vital neural systems and functions. It is only at the lofty reaches of the associative hierarchy that the question of macroscopic plasticity (as opposed to synaptic plasticity) can be meaningfully raised. The human nervous system is overwhelmingly neurospecific and dependence upon very specific patterns of connectivity is very much the rule.



Neural Plasticity

This said, at higher levels of organization neural plasticity represents the pinnacle of human mental flexibility. Leaving aside the sort of plasticity that permits you to pursue a career or to take a particular meaning from the sentence you are presently reading, some remarkable examples of neural plasticity lower in the cognitive hierarchy are also worthy of note. Although the homunculus described in question #5 is largely the result of a specific pattern of connectivity between tactile receptors and the sensory/motor cortices, damage to parts of the homuncular strips can result in a rearrangement of the homuncular map (Kimura, 1977); an example of plasticity at a fairly low level. When damage to the left hemisphere results in degraded language functions, fMRI imaging clearly shows that other brain regions (even in the right hemisphere) can adopt these responsibilities and the related language skills can be relearned (Hertz-Pannier *et al.*, 2002).



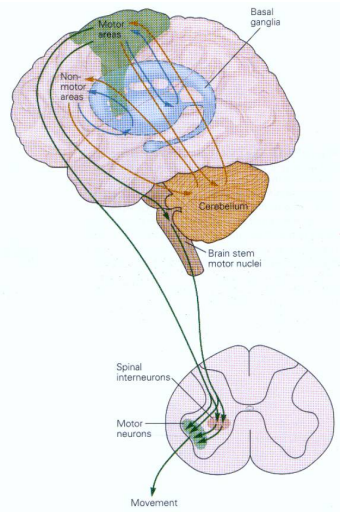
Gross Neural Plasticity

Although there is some evidence that attachment and other early experiences influence gross brain development in certain ways (Allan N. Schore, 1994; A. N. Schore, 2001), these effects are subtle (they must conserve cerebral mass, at least) and they probably contribute little to the overall plasticity of human mental faculties. Neural plasticity at the synaptic level provides the basis for the macroscopic plasticity that constitutes our intellectual flexibility within the framework of a highly neurospecific overall architecture. Macroscopic plasticity emerges from the logical networks that emerge in this framework rather than from gross anatomical change.

13) What is a fixed-action (or modal-action) pattern? How do they differ from a reflex? Describe one of each. What is the difference between a closed-loop and open-loop control circuit?

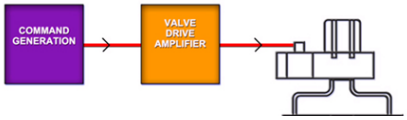
The Hierarchy of Action Patterns

Behavior of various kinds emerges from a hierarchy of sensory, motor, and cognitive systems that reflect the main phylogenetic stages in the evolution of our nervous system. The most primitive system is directly embodied in the spinal cord and its connections (first evolved in worms) followed by the hindbrain (in fish, amphibians, reptiles) and finally by the forebrain (in birds and mammals). All behaviors ultimately consist in the sequential stimulation or inhibition of reflex actions, in patterns which can be progressively diverse and flexible as they are originated higher in the nervous system hierarchy. At the bottom of the hierarchy are closed-loop reflex actions, which are automatic responses to particular types of sensory stimulation. Next in the hierarchy are fixed-action or modal responses, which are progressively more flexible and open-loop. At the top of the hierarchy are automatic and voluntary behaviors of arbitrary complexity that are coordinated over long periods of time.

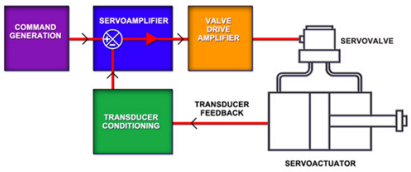


Open and Closed Loop Control Circuits

Open loop circuits operate without the benefit of feedback once they have been triggered.

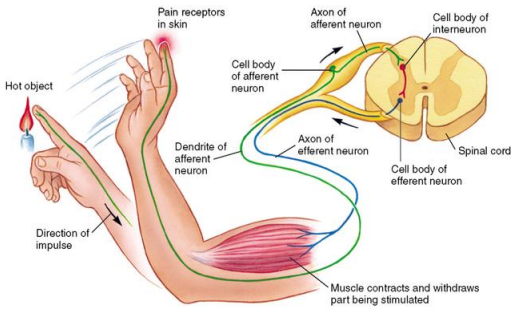


Closed loop circuits are those that rely upon feedback from sensory elements that are internal to the circuit itself.



Reflex Action

A reflex action is a closed-loop neural circuit linking stimulus to response and mediated by what is known as a reflex arc. Reflexes are normally inherent in the pattern and structure of direct neural connections, although some aspects of reflect action may reflect experience with the environment resulting in changes to synaptic potentials (they can be learned), as discussed in question # 9, above. Reflex action occurs as a direct result of appropriate sensory stimulation, much more quickly than signals can be transmitted to the brain and back. As an appropriate sensory signal is being relayed to the brain from its spinal ganglion an action potential is also generated to stimulate an effector, which triggers a movement



designed to counter the original stimulus. In this sense a reflex action is a closed-loop circuit. For example, a person touching a hot object would initiate a withdrawal reflex action in response to painful stimulus from the skin. This stimulus is transmitted to a *effector* interneuron, to which the efferent neurons are directly connected, to create an immediate muscular response that retracts the injured limb from the offensive object.

A conditioned reflex involves the modification of a reflex action in response to experience (learning). A stimulus that produces a simple reflex response becomes linked with another, possibly unrelated, stimulus as described in question #9. Pavlov's famous bell can be associated with food so that a dog will salivate (a reflex action) when it hears the bell because it has learned to associate that stimulus with food.

Fixed and Modal Action Patterns

A fixed action pattern is a complex behavioral sequence that is indivisible, and that runs to completion automatically once it has been initiated. Fixed action patterns are essentially invariant and are triggered in response to an external sensory stimulus that, unlike reflex stimuli, may be quite complex and abstract. Fixed action patterns are open-loop circuits because they are triggered by secondary stimulus and modulated, if not initiated, by higher level neural systems. Fixed action patterns that are readily apparent in human infants include rooting, sucking, postural adjustment, looking, listening, grasping, and crying in response to some very simple internal and environmental queues that come to the attention of the infant (Kagan & Herschkowitz, 2005). These action patterns are more complex than reflexes but are essentially invariant once they have been triggered.

Because some complex automatic behavioral sequences can be responsive to environmental feedback in fairly elaborate ways, at some arbitrary point of environmental responsiveness they may be referred to as modal rather than fixed action patterns, which is intended to reflect the more general nature of their execution. Modal action patterns are also complex, but are also responsive to environmental feedback during the course of their execution. The males of many species of birds engage in a specific series of elaborate movements as part of their mating behavior, which is regarded as modal action. The key stimulus for such modal action is typically the presence of a female. How well the males perform the dance is then used by females of the species to judge their fitness as a mate, which is also modal action on the part of the female. Surprisingly, since it is sensitive to social cues and can even be contagious within a group of people, yawning is also a good example of a modal action pattern (Provine, 2005).

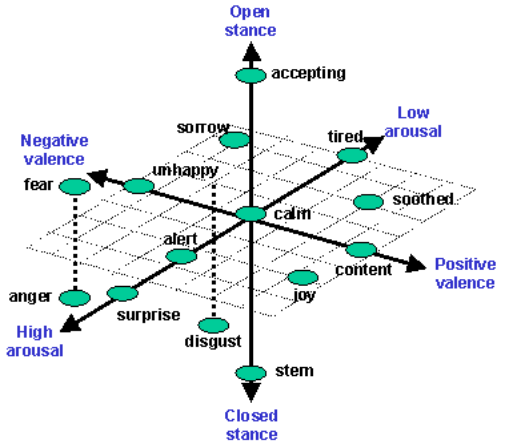
Automation of novel behavior

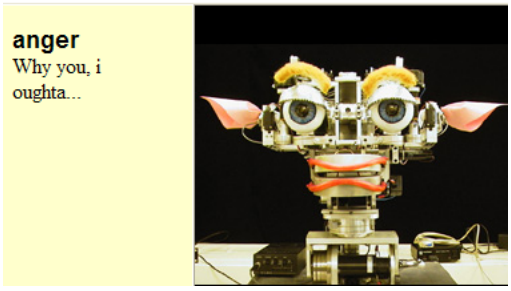
Some behavior can migrate up and down the neural hierarchy as novel elements are introduced into them on the one hand, and as they become habituated on the other. Even complex behaviors, such as driving a car, can become relatively automatic and requires little conscious attention. There is even some evidence that the right hemisphere is more involved with novel behavior, which the left hemisphere takes over as the behavior becomes habituated (Goldberg, 2001).

14) Facial expressions of particular emotions are similarly presented and recognized by many different human societies. Some emotional behaviors are also similarly expressed for humans and animals. What are some of the implications for the biogenetic bases of emotions?

Fixation of the Biogenetic Bases of Emotional Expression across Species

The association of emotional states with characteristic facial expressions and other expressive indications is universal across human cultures (Elfenbein & Ambady, 2003) and all primate species (Parr *et al.*, 2005), as well as among many other animal species. Among primates, elaborate facial communication is accompanied by specialization of brain areas that control facial movement, which is expensive and must therefore be important. The pervasive nature of expressive emotional communication and the large amount of neural architecture that is devoted to it indicates the presence of a powerful selective evolutionary pressure to maintain these expressive mechanisms as the underlying emotional systems have evolved.





The evolution of empathy, or emotional awareness, appears to have a specific neural basis in highly specialized cortical areas. The relatively large neocortex of primates generally, and of humans in particular, may have evolved specifically in order to cope with the complex demands of group living, which requires effective communication about both environmental and internal events. First in the developmental sequence and also most fundamental, effective emotional communication between infants and their caregivers is essential to the infant's immediate survival (Brazelton *et al.*, 1975; Kagan & Herschkowitz, 2005; Allan N. Schore, 1994). Although many subtleties in emotional communication are culturally defined, and therefore learned, the basics must be in place at birth and must therefore be inherent in the genetically determined neural architecture.

Emotional Communication Results in Reciprocal Activation (Attunement)

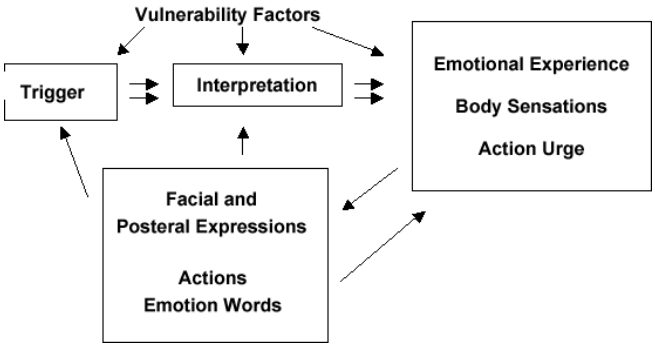
Neural models of emotion assume that emotions are caused by specialized brain systems that serve the following two basic functions:

1. Analyze the emotional meaning of stimuli by associative paring of stimulus features with innate emotion elicitors, including the emotional expressions of others.
2. Control emotional responses such as hormone release, activation of the autonomic nervous system, vocal, facial, and motor expression, allocation of cognitive resources to the situation that elicits emotion etc.

These properties of emotional brain systems suggest that the same systems that give rise to emotions are also involved in the expression of emotions and in processing the expressions of others. Emotional expression will therefore tend to result in the activation of similar brain systems in communication partners. Thus, emotional communication can be defined as a process of reciprocal activation of emotional brain systems.

Top-Down Architecture of Emotional Regulation and Expression

The evolution of the nervous system can be seen as the progressive development of a cognitive chain of command, designed to respond appropriately to the environment, with increasingly sophisticated faculties added on top of more primitive systems, exerting their influence largely by means of top-down inhibition and override. In this sense emotional regulation and expression can be seen as ***the*** central organizing principle in the biogenetic development of the nervous system. In this light, the primitive precursors of conscious emotion are the unconditioned reflexes that were discussed under question #13, above. Unconditioned reflexes can be effectively modulated by their association with conditioned stimulus, which can entrain any degree of deviation from the original response. Systematic response patterns that are coordinated by endocrinal communication systems represent the next level of integration and also the next level of potential modulation by competing emotional responses. At some point the various coordinated response patterns become accessible to conscious awareness and take on the quality of emotions as we experience them subjectively. These emotions serve as stimulus for higher cognitive faculties, which then have the opportunity to inhibit emotional responses and override them. It is apparently only at this level of emotional regulation that emotional expression can be uncoupled from the rest of the emotional response pattern, which provides the capacity for lying or acting.

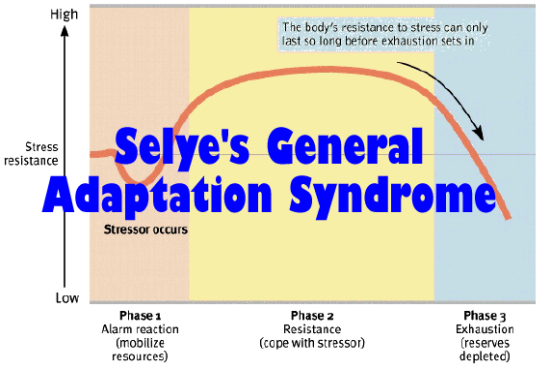


15) What are the physiological effects of stress? What is the role of the limbic system in emotion? What are thought to be the biochemical markers of aggression, and why?

Stress is the stereotypical mobilization of scarce resources, across neural and anatomical systems, in response to actual or potential challenges in the environment. On the basis of perceptual stimulus and primitive cognitive assessment of the situation, appropriate stereotypes are invoked by means of neural and hormonal signals generated largely within the limbic system, which are experienced as emotion. Emotional stereotypes can be characterized either by their subjective qualities or by their action tendencies, as in the relationship between anger and aggression. Emotional stereotypes are constituted by their specific biochemical markers and by their neurological effects.

The General Adaptation Syndrome

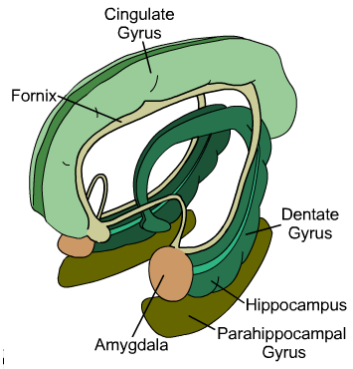
At the core of the physiological stress response is a pattern of activation known as the General Adaptation Syndrome (GAS). The GAS activates neurological and anatomical systems that are crucial for fighting or fleeing, and diverts energy to systems that may be required to act. Heart rate, blood pressure and respiration rise in order to supply muscles and brain with additional oxygen. Blood flow is diverted to the skeletal muscles and the brain and is withdrawn from the stomach, kidneys, skin and liver. Sexual and immune functions are suppressed and opiates are released into the blood in order to suppress any pain that might otherwise interfere with effective action. Natural fats and sugars are synthesized in order to provide extra energy.



The *hypothalamic-pituitary-adrenal* axis (HPA) refers to a complex set of direct influences and feedback interactions among the hypothalamus, the pituitary gland, and the adrenal or suprarenal gland. The interactions among these three organs constitute the HPA axis, which is a major functional unit of the neuroendocrine system that controls reactions to stress and regulates various body processes including digestion, immune response, mood, sexuality, and energy usage. Almost all animals have some sort of HPA axis. It is the mechanism for a set of interactions among glands, hormones and parts of the mid-brain that mediate the GAS. The hypothalamus secretes *corticotropin-releasing hormone* (CRH) and *thyrotropin-releasing hormone* (TRH), which stimulate the pituitary gland to produce adrenocorticotropic hormone (ACTH), which stimulates the adrenal glands to secrete adrenaline, noradrenaline, cortisone, cortisol. The adrenal gland is also stimulated directly with activation of the sympathetic nervous system. The thyroid gland is stimulated by the thyroid-stimulating hormone (TSH) to secrete thyroxine. The quantity of each hormone that is produced depends on the magnitude of the stressor.

The stress response results in many expenditures of energy and other limited resources that cannot be sustained indefinitely, and eventually results in a state of *adrenal exhaustion*, which has potentially serious physical and emotional consequences. In exhaustion, blood sugar levels decrease as the adrenal hormones are depleted, leading to decreased stress tolerance, progressive mental and physical exhaustion, illness and, eventually, death.

The Limbic System



The limbic system is a collection of neural structures of intermediate phylogenetic age, which are thought to be responsible for cognitive assessment and stereotypical response at the level of “inferior” mammals. In the context of the modern primate brain, these stereotypes are experienced as emotion. The limbic system is itself an extension of an even more primitive stage in neural evolution, as follows:

The *archipallium* or primitive brain, comprising the structures of the brain stem (medulla, pons, cerebellum, mesencephalon), the globus pallidus, and the olfactory bulbs. The archipallium corresponds roughly to the reptile brain, also referred to as the "R-complex" by the famous neuroscientist Paul MacLean (Maclean, 1958).

The *paleopallium*, or old mammalian brain, comprising the structures of the limbic system. The paleopallium corresponds to the brain of the inferior mammals.

The *neopallium*, or new mammalian brain, comprises almost the whole of the cortex and some subcortical nuclei. **The *neopallium*** corresponds to the brain of the superior mammals, including the primates.

The French neurologist Paul Broca first called attention to the fact that, on the medial surface of the mammalian brain, right underneath the cortex, there exits an area containing several nuclei of gray matter that he designated the *limbic lobe,* from the Latin *limbus*, which suggests the idea of a ring around the brainstem. The limbic system commands certain behaviors that are necessary for survival and it gives rise to judgments about objects and situations as being either agreeable or disagreeable. In this sense, the limbic system is the source of fundamental values and emotional valence. Emotions and feelings are mammalian inventions that originated in the limbic system. The limbic system is also responsible for some aspects of personal identity and for important functions related to memory.

Biochemical Markers of Aggression

The limbic system therefore interprets environmental stimuli at a very basic level and promotes stereotypical action tendencies that are presumably adaptive to the environment context. Since the principle mechanisms for coordinating these emotional states is an elaborate system of hormone signaling, each pattern should therefore have a characteristic biochemical signature associated with it. Several lines of evidence establish a correlation of several biochemical markets to aggressive and impulsive behavior. Research in humans and in animals suggests to a strong relationship between serotonergic dysfunction and aggression. Increased catecholaminergic activity also appears to play a role in the manifestation of aggressive behaviour. Biochemical agents such as arginine and vasopressin appear to influence impulsive aggression and abnormal testosterone levels in the blood have been regularly associated with aggressive and violent behavior (Tedeschi & Felson, 1994).

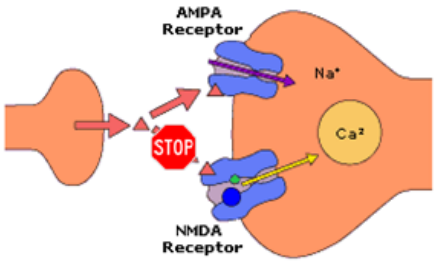
16) Some drugs modulate the formation of memory. Name one drug that usually impairs memory, and one that improves memory. Explain how the drug is thought to achieve its action, and any conditions that must be met in order to obtain the stated effect.

Memory Itself *vs.* What Is To Be Remembered

At the end of the day, memory boils down to synaptic plasticity and reinforcement mechanisms that implement the Hebb rule by adjusting the sensitivity of individual synapses (neural network nodes). All the rest is a matter of the context in which various populations of synapses are activated and reinforced. No memory can be formed until the thing to be remembered has been evoked within some neural network and reinforced, regardless of how local or distributed the network object in question. Drugs that influence mental content, attention, intensity, or salience affect memory in parallel with issues related to synaptic plasticity and long term potentiation. A fundamental distinction can therefore be drawn between drugs that influence synaptic reinforcement and those that influence contextual factors. I will offer examples of drugs that impair or improve memory in each category.

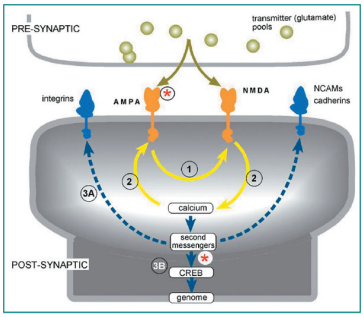
Ketamine Impairs Synaptic Plasticity by Blocking NMDA Receptors

The NMDA receptor mechanism of long term potentiation (described in question #9, above) is representative of the synaptic memory mechanism in general, and ketamine is offered as an example of a drug that generally impairs long term memory formation at that level. Ketamine is a veterinary anesthetic that is also used as an illicit recreational drug because of its psychedelic properties. It has been demonstrated to result in heterogeneous impairment of memory formation, which is thought to result from a permanent blockage of the NMDA receptor as a secondary effect resulting from the synthesis of an enzyme that serves as an irreversible NMDA inhibitor, sealing the calcium channel in the post-synaptic membrane and blocking the process that results in Hebb reinforcement at that synapse (Honey *et al.*, 2005; LaPorte *et al.*, 2005; Parwani *et al.*, 2005). Memory cannot be formed at the synaptic level when the NMDA channel is irreversibly blocked in this way.



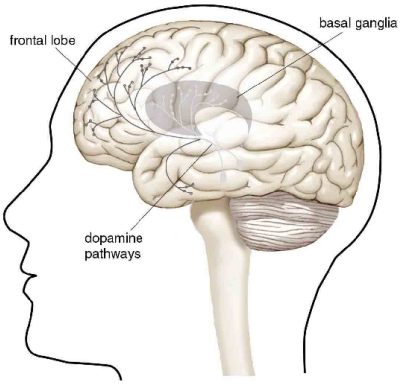
Ampalex Improves Memory by Enhancing AMPA Receptors

Ampalex is offered as an example of a drug that generally enhances memory at the synaptic level by enhancing the sensitivity of AMPA receptors directly as well as by facilitating the calcium process that is at the heart of the NMDA reinforcement mechanism described in question #9, above. Such enhancement has the effect of enhancing memory formation generally in situations where AMPA sensitivity has been reduced by some pathological condition, such as Alzheimer's and does not improve memory in normal subjects (Hampson *et al.*, 1998).



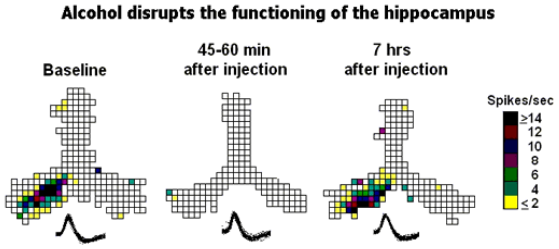
Amphetamines Improve Memory by Boosting Prefrontal Dopamine Activity

In order to remember something it must first be represented in working memory, and conditions which disrupt attention or cognitive coherence, such as schizophrenia, bi-polar disorder, and ADHD, all are associated with heterogeneous memory impairments. These conditions are also associated with deficiencies in the dopamine pathways to the prefrontal cortex, which are known to mediate cognitive reinforcement and, presumably, memory formation. Amphetamines of various kinds that are used to treat these disorders have been shown to improve memory, probably by stimulating dopamine activity in the prefrontal cortex (McKetin & Mattick, 1998; Simon & Setlow, 2006; Soetens *et al.*, 1993). This interpretation is supported by the finding that amphetamines are not associated with memory enhancement in normal controls who do not display cognitive deficits to begin with.



Alcohol Impairs Memory by Hippocampal Anesthesia

Alcohol impairs memory formation by means of general suppression of activity in the hippocampus (anesthesia) (White *et al.*, 2000). This discovery was based on the observation that acute alcohol exposure produces a syndrome of memory impairment similar to the impairment that is produced by hippocampal damage. Specifically, both acute alcohol exposure and hippocampal damage impair the ability to form explicit memories but do not affect short-term memory storage or, in general, the recall of information from long-term storage. The mechanism for this impairment appears to be the general suppression of CA1 pyramidal activation across the hippocampus rather than any synaptic effect. Alcohol impairment of memory is largely the result of influence (sedation) on a particular cerebral context (hippocampal activation).

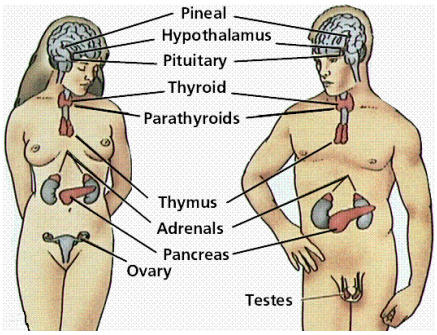


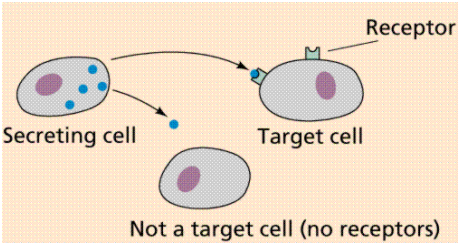
Psychedelics Enhance Memory of Sensory Gestalts

I cannot find any scientific evidence that I can cite to support the contention that psychedelic drugs enhance the memory of sensory gestalts, but anyone who went to the University of California at Santa Cruz during the 70's can testify that this is the case. Thirty years later I can still recall, in exquisite multi-sensory detail, numerous scenes that I experienced while under the influence of psychedelic drugs during that period; scenes which are unremarkable in any respect that I can identify, other than their remarkable sensory emphasis. I surmise that this is due to the distinctive and unusual quality of those experiences rather than to any systematic effect that psychedelics might have on the mechanics of synaptic plasticity. I surmise that this is the central mechanism of the psychedelic "flashback" (Wesson & Smith, 1976).

17) What are hormones, where are they produced, what is their function, and how do they work? How do peptide, amine, and steroid hormones differ? How are secretion rates monitored and controlled?

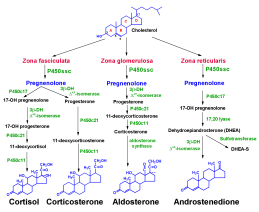
Whereas the nervous system coordinates rapid and precise responses to stimuli by means of action potentials, which are essential digital signals (see question #3, above), the endocrine system maintains homeostasis in various vital systems by means of chemical signals that are disbursed by the bloodstream and other fluid networks. The endocrine system also works in parallel with neural mechanisms to control the growth and maturation of various anatomical systems and of the organism as a whole. The endocrine system is a collection of glands that secrete chemical messengers known as hormones, which are distributed through the blood or other fluid systems to target cells that self-select by means of their matched receptors, which can be extremely specific. For this reason, a variety of distinct hormone classes have evolved to address distinct systems which overlap with one another physically, because they all require blood, interstitial fluid, or other fluid resources that are systemically disbursed.



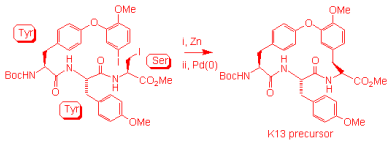


Hormones are grouped into three classes (steroid, peptide, and amine) based on their chemical structure:

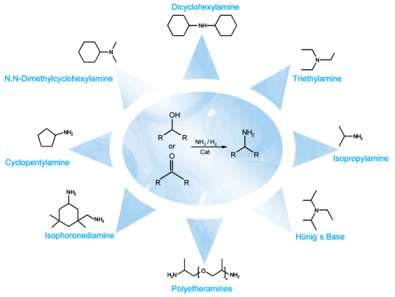
Steroids are lipids, which are derived from cholesterol. Testosterone is the male sex hormone and estradiol, which is similar in structure to testosterone, is the female equivalent. Steroid hormones are secreted by the gonads, adrenal cortex, and placenta. Once synthesized, steroid hormones pass directly into the bloodstream and they are not stored by cells, so that the rate of synthesis entirely determines their concentration in the blood.



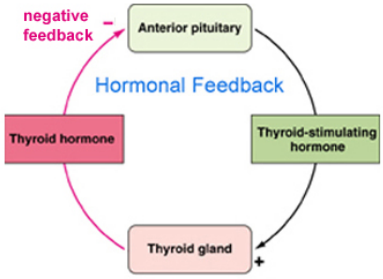
Peptides are short chains of amino acids, which constitute the majority of hormones. Peptides are synthesized by the pituitary, parathyroid, heart, stomach, liver, and kidneys as precursor molecules that are further processed by cells in the *endoplasmic reticulum,* where they are stored until their release is triggered by "master" hormones that are synthesized primarily in the pituitary. Different hormones can often be synthesized from the same precursor molecule by combination with different enzymes.



Amines are derived from the amino acid tyrosine and are secreted from the thyroid and the adrenal medulla. Amine hormones (notably epinephrine) are stored as granules in the cytoplasm until needed. Amines are frequently involved in initiating and terminating growth processes, particularly with regard to gross anatomy.



More than 50 hormones in these three categories are synthesized by various endocrine glands throughout the lifespan. As discussed in question #3, above, the endocrine system relies on negative feedback to regulate the production of hormones in order to maintain homeostasis in various physiological functions. Negative feedback regulates the secretion of almost every hormone. Cycles of secretion maintain physiological and homeostatic equilibrium. These cycles can range from hours to months in duration.



There are two fundamental mechanisms by which hormones affect change within target cells:

Activation of enzymes and other dynamic molecules: Most enzymes shuttle between conformational states that are catalytically active versus inactive, on versus off. Many hormones affect their target cells by inducing such transitions, usually causing an activation of one of more enzymes. Because enzymes are catalytic and often serve to activate additional enzymes, a seemingly small change induced by hormone-receptor binding can lead to widespread consequences within the cell.

Modulation of gene expression: Stimulating transcription of a group of genes clearly can alter a cell's phenotype by leading to a burst of synthesis of new proteins. Similarly, if transcription of a group of previously active genes is shut off, the corresponding proteins will soon disappear from the cell.

Hormone receptors can be categorized into one of two types, based on their location within the cell:

Cell surface receptors: Proteins and peptides, catecholamines and eicosanoids. Generation of second messengers which alter the activity of other molecules within the cell

Intracellular receptors: Steroids and thyroid hormones alter transcriptional activity of responsive genes.

Location of Receptor	Classes of Hormones	Principle Mechanism of Action
Cell surface receptors (plasma membrane)	Proteins and peptides, catecholamines and eicosanoids	Generation of *second messengers* which alter the activity of other molecules - usually enzymes - within the cell
Intracellular receptors (cytoplasm and/or nucleus)	Steroids and thyroid hormones	Alter transcriptional activity of responsive genes

18) What are the major classes of psychoactive drugs, and what are their most common applications?

Psychoactive drugs can be classified into the following major categories:

***Antianxiety agents**:* These include benzodiazepines such as alprazolam (Xanax), lorazepam (Ativan), diazepam (Valium), and chlordiazepoxide (Librium), and other medications including buspirone (BuSpar) and paroxetine (Paxil). Antianxiety agents are also known as minor tranquilizers. Other drugs used to treat anxiety include buspirone, some antidepressants, and barbiturates

Anxiety can be defined as persistent nervousness, tension, or panic caused by stress or other psychological causes. Antianxiety drugs promote relaxation or reduce the physical symptoms of anxiety by depressing the central nervous system. Benzodiazepines are also used to treat insomnia. A class of antianxiety agents called beta-blockers reduces the shaking or palpitations that are sometimes associated with panic episodes.

***Antidepressants**:* For treatment of major depressive disorder, dysthymic disorder, and bipolar disorder. These include venlafaxine (Effexor), nefazodone (Serzone), bupropion (Wellbutrin), MAOI inhibitors such as phenelzine (Nardil) and tranylcypromine (Parnate); selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine (Prozac), paroxetine (Paxil), and sertraline (Zoloft); tricyclic antidepressants such as amitriptyline (Elavil), doxepin hydrochloride (Sinequan), desipramine (Norpramin), and perphenazine/amitriptyline combinations (Etrafon).

Depression is associated with imbalance in the level of certain neurotransmitters in the brain and antidepressants moderate the levels of these chemicals in the synaptic mechanism. Tricyclic antidepressants and serotonin reuptake inhibitors (e.g., fluoxetine or sertraline) prevent cells from absorbing certain neurotransmitters, which increases their levels in the synapse. Monoamine oxidase inhibitors increase neurotransmitter levels by interfering with the enzymes that break them down.

***Antimanic agents**:* For treatment of mania associated with bipolar disorder. Includes divalproex sodium (Depakote) and lithium carbonate (Lithium, Eskalith, Lithobid, Tegrator).

***Antipanic agents**:* For treatment the panic symptoms that are associated with many anxiety disorders. Includes clonazepam (Klonopin), paroxetine (Paxil), alprazolam (Xanax), and sertraline (Zoloft).

Antipsychotic agents: Also known as neuroleptic agents. For treatment of psychosis related to schizophrenia, delusional disorder, and brief psychotic disorder. Includes clozapine (Clozaril), haloperidol (Haldol), loxapine (Loxitane), molindone (Moban), thiothixene (Navane), risperidone (Risperdal), and olanzapine (Zyprexa); also includes phenothiazines such as prochlorperazine (Compazine), trifluoperazine hydrochloride (Stelazine), and chlorpromazine (Thorazine).

Most antipsychosis drugs work by inhibiting dopamine activity in one way or another. Antipsychotics typically reduce the effect of dopamine by blocking the nerve cell receptors that respond to the chemical. Antipsychotics also interfere with the activity of acetylcholine.

Obsessive-Compulsive Disorder agents. For treatment of OCD. Includes fluvoxamine (Luvox), paroxetine (Paxil), fluoxetine (Prozac), and sertraline (Zoloft).

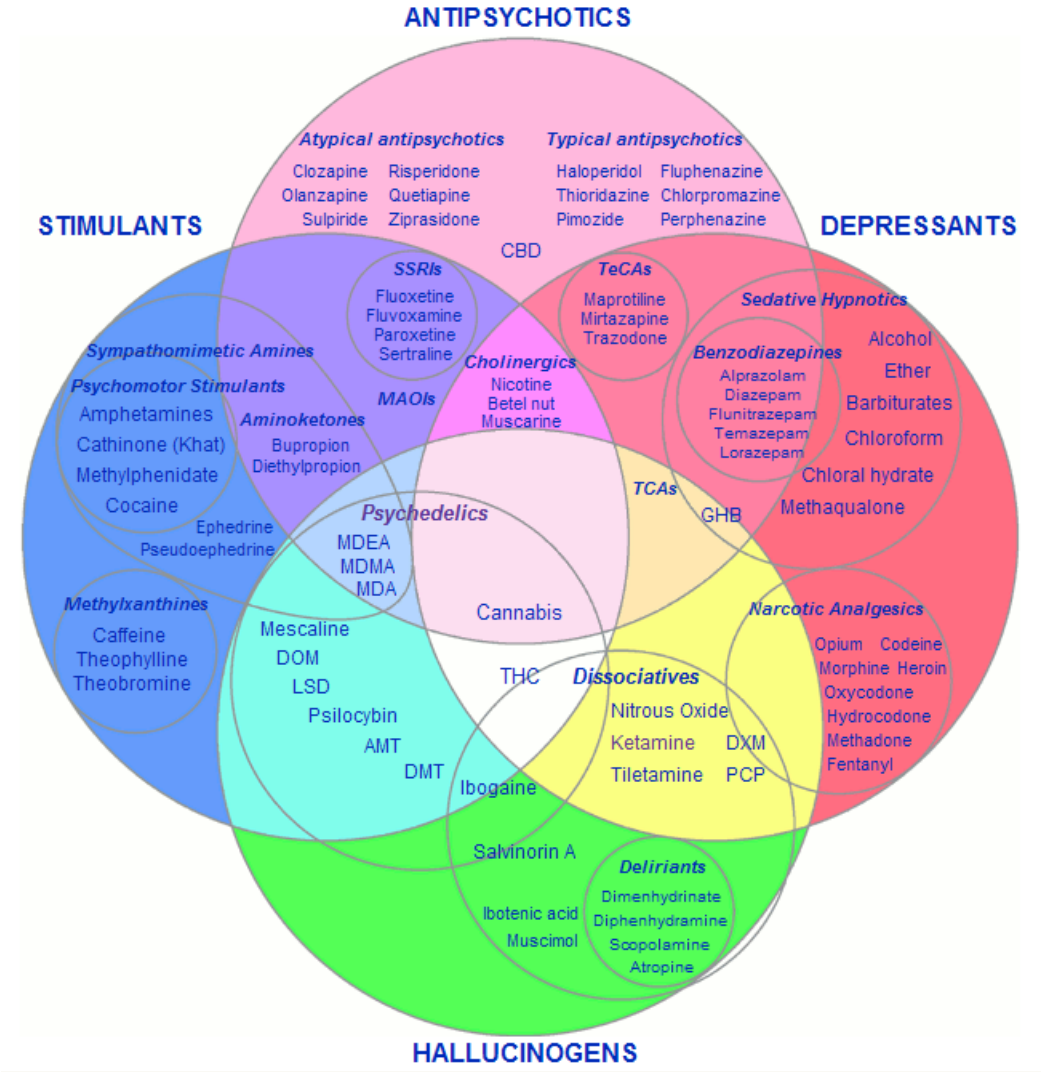
Stimulants: For the treatment of attention deficit disorders (ADD and ADHD) and narcolepsy. They include methylphenidate hydrochloride (Methylin, Ritalin) and methaamphetamines (Desoxyn, Dexedrine, and DextroStat). Also includes nicotine, which is the principle active ingredient of tobacco. Illicit counterparts include amphetamines and cocaine.

Opiates: For treatment of pain, but widely abused in both prescription and illicit forms. Includes morphine, heroin, codeine, hydrocodone (Vicodan), and meperidine (Demerol).

Psychedelics: No established therapeutic uses, psychedelics produce profound alterations in perception. Includes mescaline, LSD, and psilocybin.

Cannabinoids: Therapeutic use is disputed for treatment of eating disorders, pain, and depression. The most notable cannabinoid is delta-9-tetrahydrocannabinol, the psychoactive substance in marijuana.

Ethanol: Ethanol is the alcohol in beer, wine and hard liquor, and is one of the most popular psychoactive drugs.



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